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Drug and Cosmetic Industry

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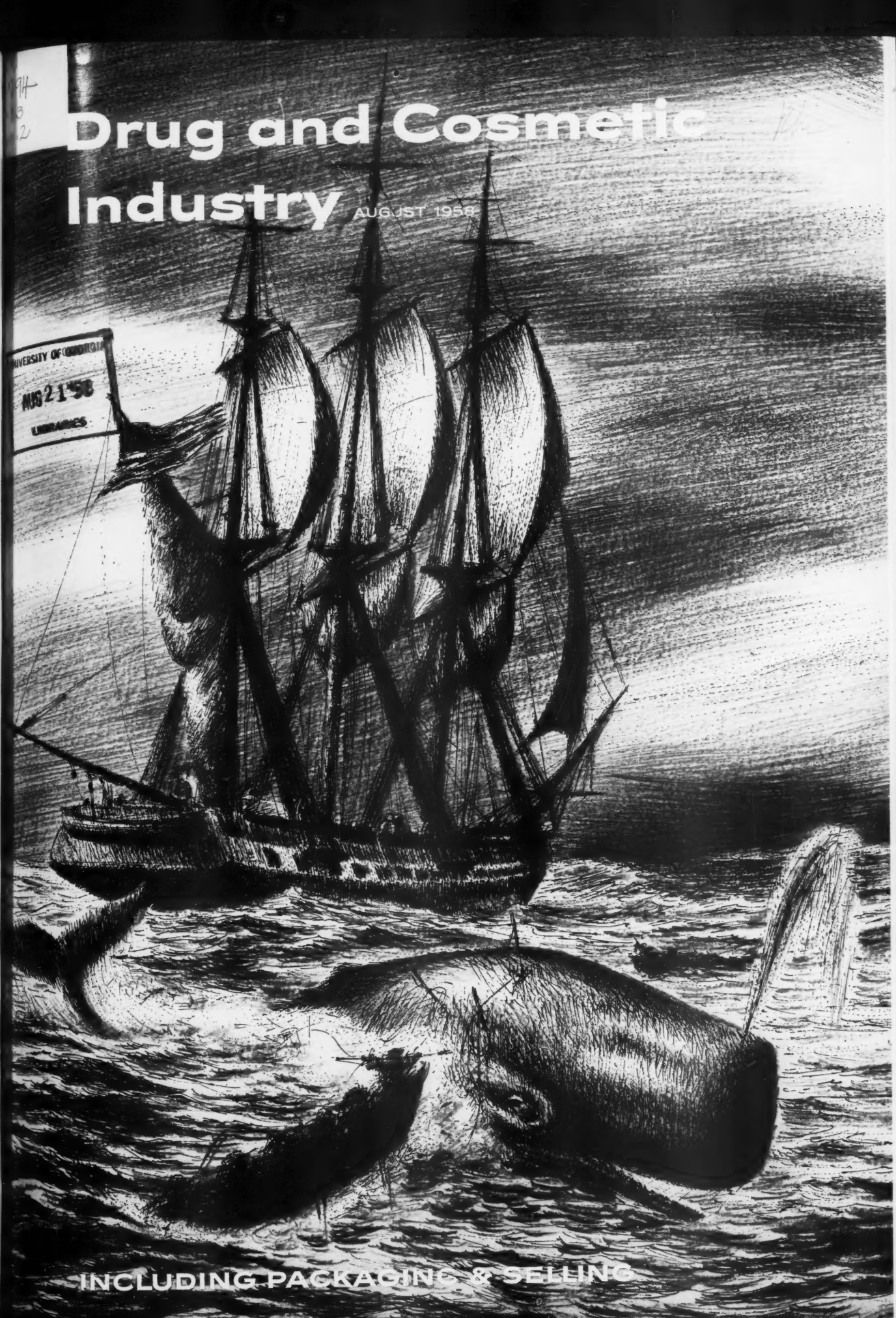

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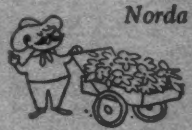

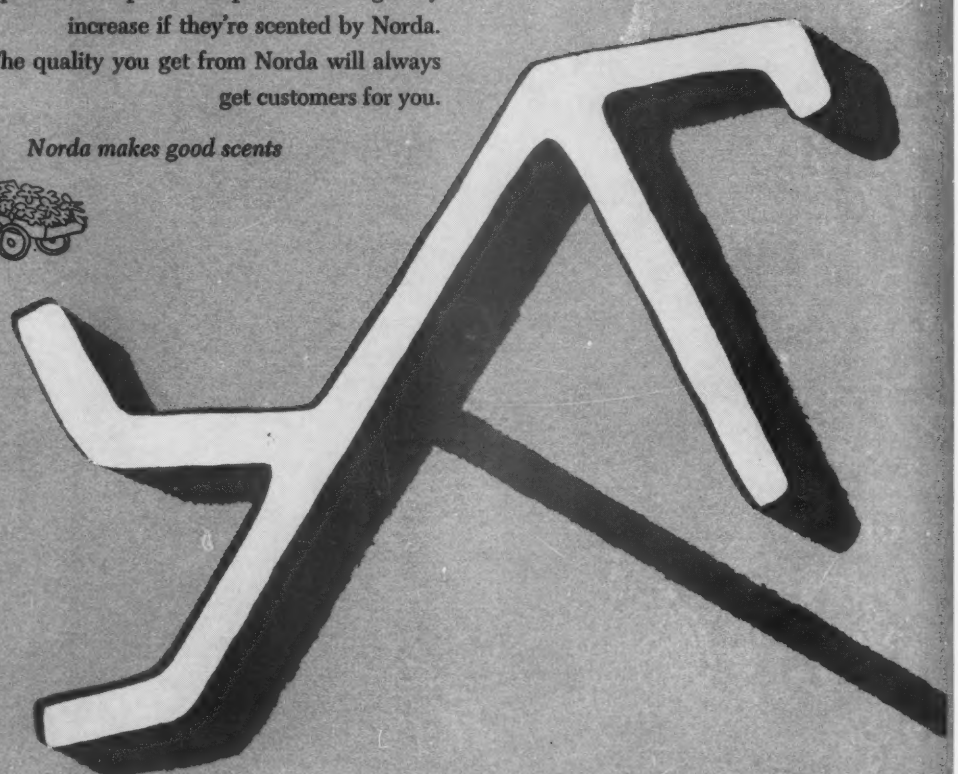

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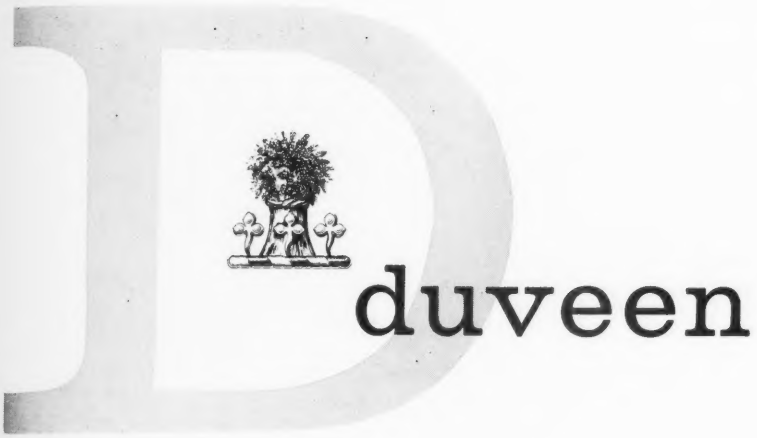

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Drug and Cosmetic Industry

Contents **August 1958 Vol. 83 No. 2**

Cover by Joel

Feature Articles

155 **Kanamycin**
by Joseph Kalish, Ph.D.

158 **The New Colliere Factory**
by Francis Chilson

160 **Solubilization by Means of Lanolin Derivatives**
by Lester I. Conrad, Kalmen Motiuk and Henry F. Maso

162 **Rouges**
by Morton Daniels

164 **Regulation of Biologicals**
by Parke M. Banta

166 **Hard to Get African Rarities**
by Steffen Arctander

168 **The Study of Human Horny Layers**
by Peter Flesch, M.D., Ph.D.

Packaging and Selling Section

173 **The Well-Conceived Ethical Package**

177 **Packaging and Selling**
by Frazer V. Sinclair

182 **Packaging News**

185 **D & C Advertising News**
by Ted Klein

Departments

147 **Keeping Posted**
by Thomas R. Farrell

188 **Patent Thoughts and Trends**
by Thomas Cifelle, Jr.

193 **News**

205 **Management Forum**
by Francis Chilson

214 **Industry's Books**
by Harry G. Kelbly

231 **Trade Literature**

Technical Abstracts

by Joseph Kalish, Ph.D.

217 **Advancing Therapy**

220 **Perfumer's Shelf**

223 **Compounder's Corner**

227 **Skin Research**

233 **Readers' Questions**

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Drug & Cosmetic Industry is published monthly by Drug Markets, Inc., Frazer V. Sinclair, President and Treasurer; Thomas R. Farrell, Vice-president and Secretary. Editorial and General Office: 101 West 31st St., New York 1, N. Y., U. S. A. Publication Address: Sun Printing Corp., 28 Renne Ave., Pittsfield, Mass., U. S. A.

Business Manager, Frazer V. Sinclair; Advertising Manager, P. W. Alexander; Advertising Representatives, Walter M. Brauneiss, C. R. Keeley; Production Manager, Katherine Hyde; Circulation Manager, Harry G. Kelbly.

Midwestern Advertising Representative: Dwight Early and Sons, 100 No. LaSalle St., Chicago 2, Telephone, CEntral 6-2184.

Subscription price $3.00 a year, in advance. Foreign Countries, $5.00. Single copies, 35c; Back issues 50c. Entered as Second Class Matter, January 1, 1928 at the Post Office at Pittsfield, Mass., under the Act of March 3, 1879. Member of Audit Bureau of Circulation.

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FELTON'S NEW LINE OF COMMAND . . . MASCULINE SCENTS

For men only—Felton's vigorous new perfume group is yours to command. Again, Felton's unique combination of experience, skill and instinct has achieved the unmistakable *eau de success*. Here are all the lures you require for tracking down today's tremendous masculine market.

For big game . . . **Beau Brummel #1256,** a he-man odor with distinctive woody, dry bottom note. **Esquire S.T. #20** and **Esquire Country #20** appeal to aristocratic tastes, an original aroma with beautiful dry notes.

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Perfume compounders will find Felton's new bases stimulating tools for building new compounds or for improving existing lotion, talc or aerosol scents:

Adamal, rich in fine woody notes, dryness tinged with precious resinous notes. **Brummel Base #1156** can be used from 5-15% in existing compounds for a woody-dry bottom note of strong masculine appeal. **Aldicuir,** a unique "natural" base with rich, true leather note.

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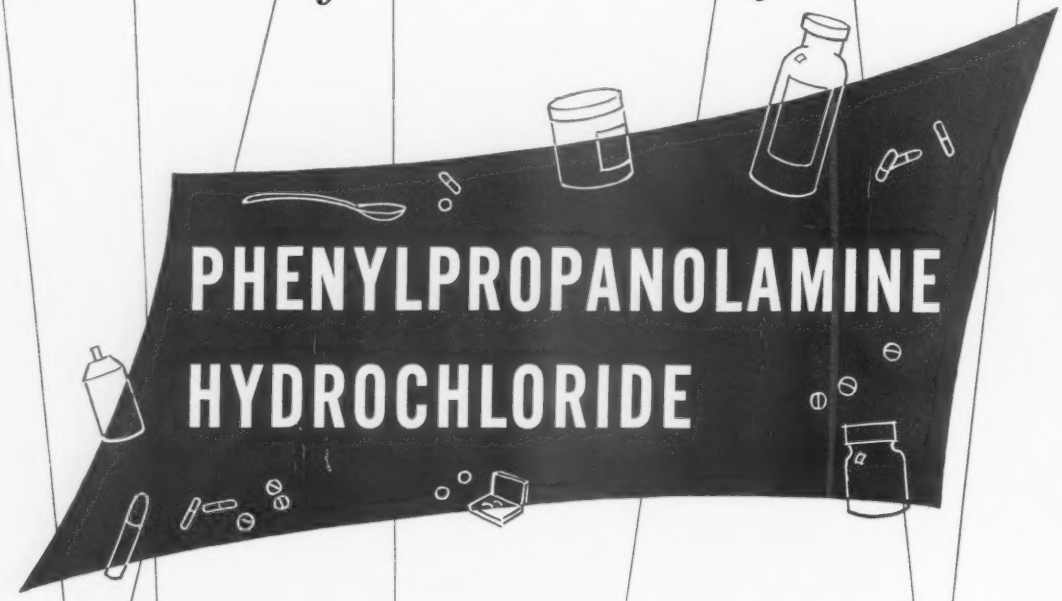

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Because of fast-growing interest in this drug, NYQ has installed extensive new facilities to assure continuing bulk production of a high quality material. Stocks are ready now for immediate shipment from five coast-to-coast warehouse points.

As a nasal decongestant, phenylpropanolamine hydrochloride gives convenient relief to cold and allergy sufferers since it is highly effective when taken orally. It can be incorporated ...with or without antihistamines...in cough syrups, tablets and other cold remedies as well as in sprays and inhalators.

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In the stomach, stubborn integrity;

in the intestine, swift dissolution—

en français, an accolade for

cellulose acetate phthalate

In Paris, the City of Light, at 23, rue de l'Ecole-de-Médecine, there has been published a brochure bearing the title, "Les enrobages modernes des dragées et des pilules." It devotes itself in part to cellulose acetate phthalate, a substance of our invention.

States this magnificent document (as inadequately rendered into the English tongue by our own poor efforts):

"But the largest part of our work was reserved for cellulose acetate phthalate. This product is extremely insoluble in the acid solutions and its solubility in pancreatic medium is due in part to a fermenting action which can be produced independently of pH, but can equally work in an alkaline medium. According to the fine demonstration of our co-worker, (name omitted in this quotation from considerations of privacy), **cellulose acetate phthalate is an ester which is hydrolyzed by esterase with a formation of acetic and phthalic acids and this explains all the interest in this new coating.**

"We believe we have demonstrated that it combines all the qualities required of a true enteric coating: First, it is devoid of all toxicity; Second, the formula which we have used combines the conditions for forming on a core a coating layer of uniform distribution.

"Moreover, the numerous experiments effected, 'in vitro' and 'in vivo' gave absolutely corresponding results and demonstrated that: thirdly, acetate phthalate coating resists perfectly prolonged passage in the stomach surpassing, by far, even the base criteria which we have established.

"Fourthly, it disappears very rapidly in an intestinal medium and in a lapse of time which we may estimate as under a half hour, whether the medium be alkaline or acid. This last peculiarity, characteristic of acetate phthalate, ranks this coating incontestably at the head of all those which we have tried and allows us to conclude that among these it is practically the only one responding exactly to the requirements of the trade.

"Two important factors remain which we must not overlook in that they concern the pharmaceutical industry. Fifthly, the technique of applying this coating is extremely simple and rapid, and sixth, its price is slightly higher than that of other enteric coatings, but it remains within the normal limits and does not otherwise appreciably influence the cost of manufacture."

We shall gladly and at our own expense provide a translation of fifty pages from this comprehensive study of enteric coatings. Our distribution of the translation is not to be construed as adopting or recommending anything said or reported therein. Legal personalities stress this point.

The true, genuine Eastman Cellulose Acetate Phthalate (which has been applied to well over a billion doses during the past 18 years) bears the trademark "C-A-P." For the translation, procedural bulletin, descriptive folder, and prices, write ***Distillation Products Industries,*** Rochester 3, N. Y. Sales offices: New York, Chicago, and Memphis • W. M. Gillies, Inc., West Coast • Charles Albert Smith Limited, Montreal and Toronto.

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some 3700 Eastman Organic Chemicals for science and industry

Distillation Products Industries *is a division of* **Eastman Kodak Company**

A MUST FOR ALL

MOST POTENT VITAMIN

CYANOCOBALAMIN

AT ALL AGES

PRODUCT POSSIBILITIES

Market	Size	Sales Potential (Multivitamins)	Cyanocobalamin (Vitamin B_{12}) Provided Daily
PRENATAL	More than 4,000,000	More than $100,000,000	Up to 25 micrograms
INFANT	More than 8,000,000 (less than 2 years old)	More than $120,000,000	Up to 25 micrograms
CHILDREN AND ADOLESCENTS	More than 50,000,000	More than $600,000,000	Up to 25 micrograms
PATIENTS UNDER STRESS*	In the millions	In the multimillions	Up to 25 micrograms
"40-PLUS"	Nearly 60,000,000	More than $0.5 billion	Up to 10 micrograms
"65-PLUS" (GERIATRIC)	14,000,000 —Plus	$400 million —Plus	Up to 25 micrograms

*...and prolonged

© Merck & Co., Inc.

New Discoveries About Vitamin B_{12} (Cyanocobalamin) Renew and Enhance Medical Interest in All Vitamins

New product possibilities and market potentials for Vitamin B_{12} and Multivitamins are steadily on the increase . . . by virtue of a veritable flood of nutritional and clinical reports from a multitude of researchers exploring the manifold significance of Cyanocobalamin. Vitamin B_{12}* is the most potent vitamin—physiologically, clinically, and commercially . . .

12 BASIC REASONS FOR EXPANDING B_{12} MARKETS

As you can note in the tabulation of **PRODUCT POSSIBILITIES** (page opposite), the markets and sales potentials for modernized Multivitamins providing optimal levels of Cyanocobalamin are indeed vast. To explain why these potentials are so great and are still growing, here are 12 major highlights from today's news about the most newsworthy vitamin:

1. Vitamin B_{12} is a vital factor in basic metabolic processes, including synthesis of nucleoproteins.

2. Cyanocobalamin is essential for human nutrition at all ages.

3. It is required for normal production and maturation of red cells, at all ages—hence for prevention of pernicious anemia.

4. The integrity of the oral and gastrointestinal epithelium is vitally dependent upon an adequate intake of this vitamin.

5. It is required for the metabolic processes involved in the functional integrity of myelinated fibers in the central nervous system and peripheral nerves.

6. A vital factor in general health and vigor, vitamin B_{12} intake must be adequate to prevent ultimate physical and mental deterioration, as manifested in pernicious anemia.

7. **NEVER DISPENSABLE!** The oral requirement for normal non-pregnant adults has been estimated to be about 5 micrograms daily, while the parenteral requirement is thought to be 1 microgram.

8. Because of their greater metabolic demand, children may require relatively much more Cyanocobalamin than adults.

9. Possibly, "hidden hurt to the unborn" (such as congenital malformation) may result if significant vitamin B_{12} deficiency develops **EARLY** in pregnancy.

10. Many **GERIATRIC** patients have been found to have low blood levels of vitamin B_{12}—supplementary vitamin B_{12} may be indicated.

11. **IN STRESS:** Considerable evidence favors the view that vitamin B_{12} may be one of the vitamins the requirement for which is increased by serious, prolonged stress.

12. **IN NUMEROUS DISORDERS,** multivitamins with high levels of Cyanocobalamin are being used by physicians who are convinced that extraordinary stress increases vitamin needs.

OUTSTANDING ADVANTAGES OF CYANOCOBALAMIN U.S.P.

Cyanocobalamin U.S.P. is Crystalline Vitamin B_{12}, with officially recognized U.S.P. status. Crystalline Vitamin B_{12} is outstandingly safe—it is best for parenteral administration because virtually free from side effects.

Clinical acceptance has been clearly established: Cyanocobalamin U.S.P. was used in the majority of the published clinical studies on the value of Vitamin B_{12}. Moreover, because of precise uniformity, pharmaceutical behavior determined on one lot of Crystalline Vitamin B_{12} will be true on all successive lots. And, in certain formulations the crystalline form of the vitamin is more stable than the concentrate.

Thousands of physicians have been impressed by the Merck Crystalline Vitamin B_{12} exhibit and the new 72-page exhibit booklet spotlighting the safety of Cyanocobalamin U.S.P.: "For the benefit of your patient, insist on Crystalline Vitamin B_{12} —i.e., the only Cyanocobalamin U.S.P. . . . Make sure that Cyanocobalamin U.S.P. is on the label."

MERCK SERVICES— MULTIPLE AND UNIQUE

First with Vitamin B_{12} as well as other vitamins, Merck celebrates in 1958 the eleventh anniversary of the discovery of Cyanocobalamin by Merck researchers.

For more than a decade Merck has steadily expanded its progressive technical investigations of every facet and every application of the most potent vitamin. Vast data have been amassed and kept up to date as regards clinical experience, new product development and every type of problem involved in analysis, labeling, and marketing of Vitamin B_{12} preparations.

Now Merck Production supplies Crystalline Vitamin B_{12} and Cobalamin Concentrate in a full selection of types—plus an extensive variety of the other vitamins.

In addition here are five uniquely helpful Merck services to automate your vitamin marketing:

1. Merck-sponsored Research creates new applications for your vitamin products.

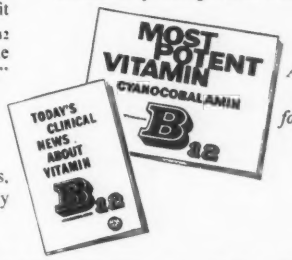
2. The Merck Memo news-features help to spark your ideas for new vitamin products.

3. Merck Literature Service (now exceeding 100 pieces on vitamins) is designed to aid your product development staff.

4. The Merck Technical Service staff is ready to assist you on problems in formulation, compatibilities, labeling, and specialized control procedures you may need to guard your product quality . . .

5. Merck Promotion is building nation-wide physician interest in—and acceptance of—YOUR vitamin products. Merck exhibits and exhibit booklets pre-sell your Vitamin B_{12} products.

If you are planning any product development involving the most potent vitamin or any other vitamin, you'll be underway faster and with fewer headaches by calling Merck **FIRST.**



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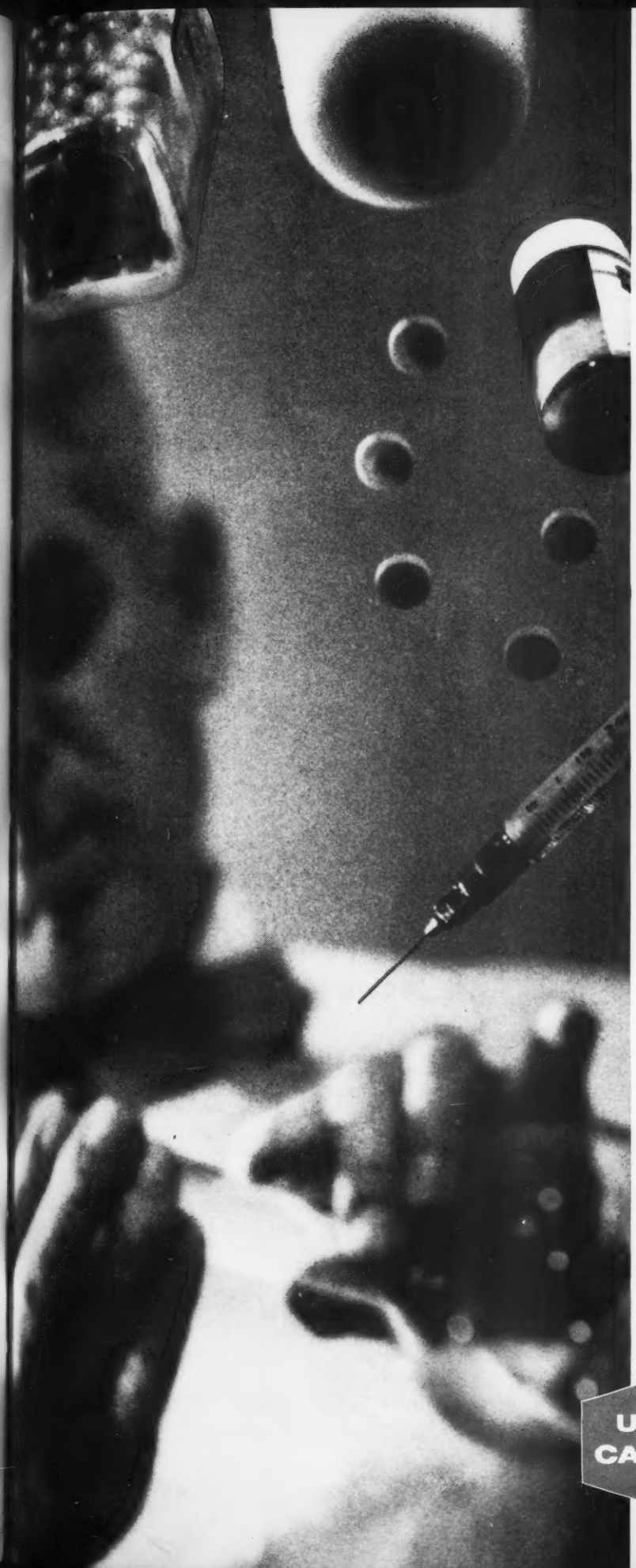

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Here are ten anhydrous, water-soluble compounds that make effective, low-cost vehicles and carriers for your medicaments.

In tablet formulation, CARBOWAX polyethylene glycols shorten wetting and drying processes as well as costly double compression. They also make ideal non-caloric tablet coatings that can be applied in half the time required for sugar coating.

Ointments based on CARBOWAX polyethylene glycols spread on evenly and adhere well even if the skin is moist. And, ointments based on CARBOWAX polyethylene glycols can be quickly and easily removed with a water rinse.

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Find out how these unusual materials can improve your profit picture. Write for the newly-published booklet, "CARBOWAX polyethylene glycols." Write . . . Department B, Union Carbide Chemicals Company, Division of Union Carbide Corporation, 30 East 42nd Street, New York 17, New York.

"Carbowax" and "Union Carbide" are registered trade marks of UCC.

UNION CARBIDE CHEMICALS

News about

B.F.Goodrich Chemical *raw materials*

Photos show strong gel — heavy silver spoon is suspended. Also easy stirring — you can do it with a feather. Try this test for yourself.

mucilages of CARBOPOL® 934 give high viscosity with easy handling

MAKE the spoon and feather test—prove this ideal combination of manufacturing advantage and end-product benefit. Mucilages of neutralized Carbopol 934 give you high viscosity combined with real ease of stirring and pumping. The end product has excellent spreading qualities.

It is highly compatible with materials most frequently used in cosmetic, pharmaceutical and industrial compounds using water base dispersions. Carbopol 934 retains viscosity better than natural or other synthetic polymers—at room temperatures, elevated temperatures, during prolonged aging periods and in the presence of bacteria and fungi.

Samples are available, also a new booklet that tells all the advantages of Carbopol 934. Write to Dept. RB-4, B.F.Goodrich Chemical Company, 3135 Euclid Avenue, Cleveland 15, Ohio. Cable address: Goodchemco. In Canada: Kitchener, Ontario.

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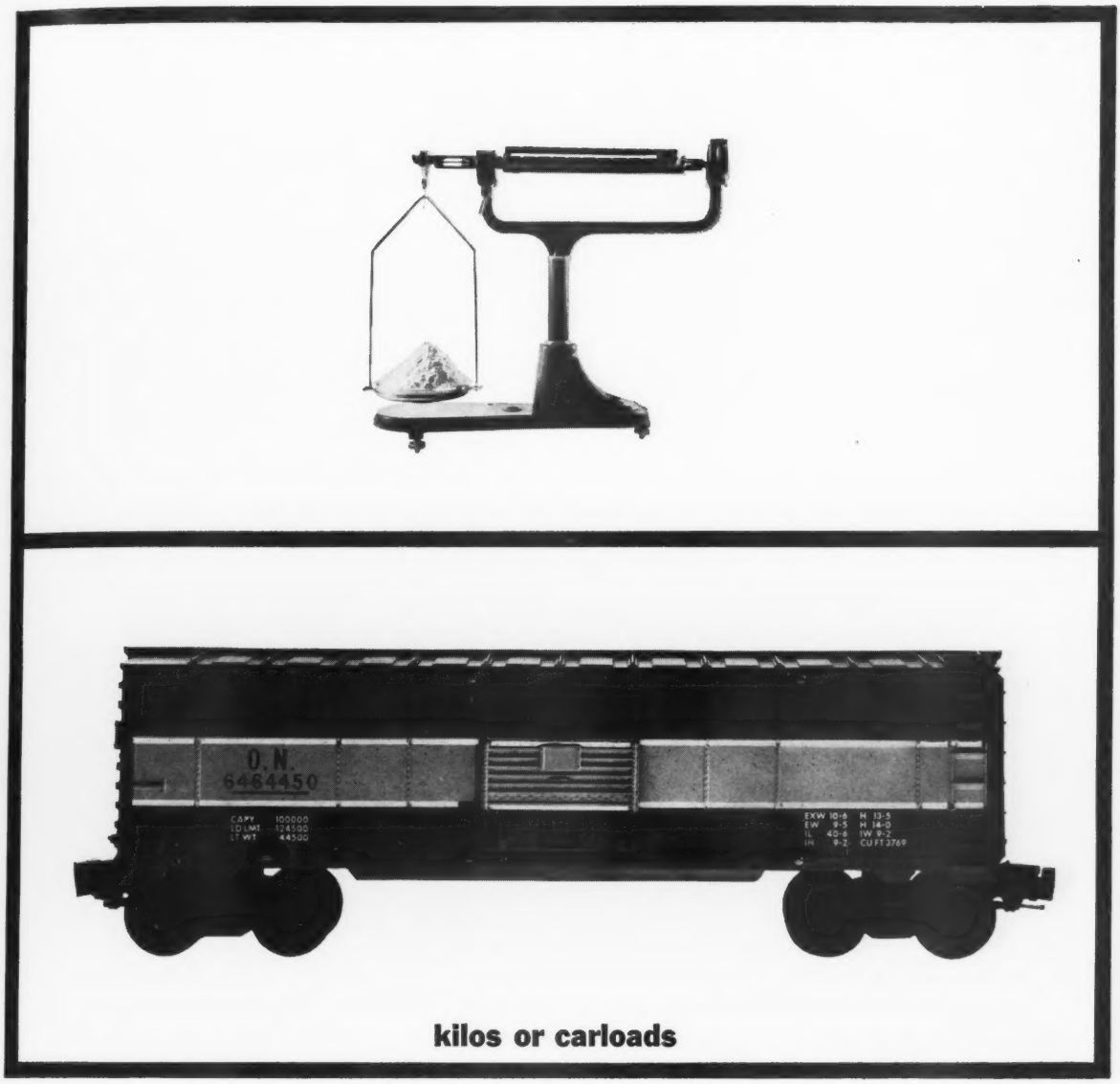

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fine quality in bulk pharmaceuticals

FOR YOUR VITAMIN MANUFACTURING NEEDS, The Upjohn Company now offers folic acid in bulk – yet made in accordance with the same exacting standards of quality that have characterized Upjohn fine pharmaceuticals for almost seventy years. Upjohn Folic Acid is 99% pure by both chemical and microbiological assays. Its potency and purity are assured by several tests performed *in addition* to U.S.P. specifications.

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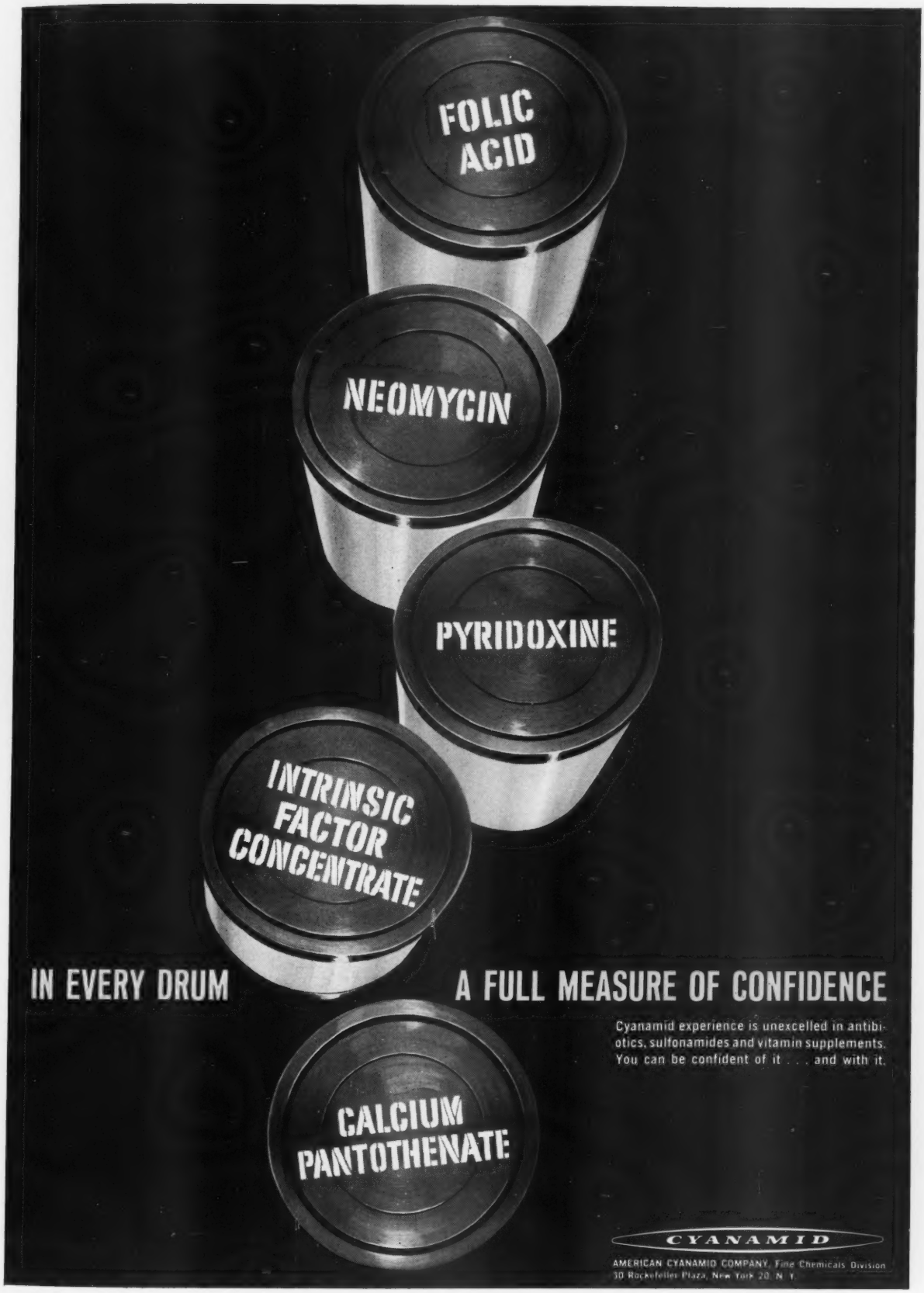

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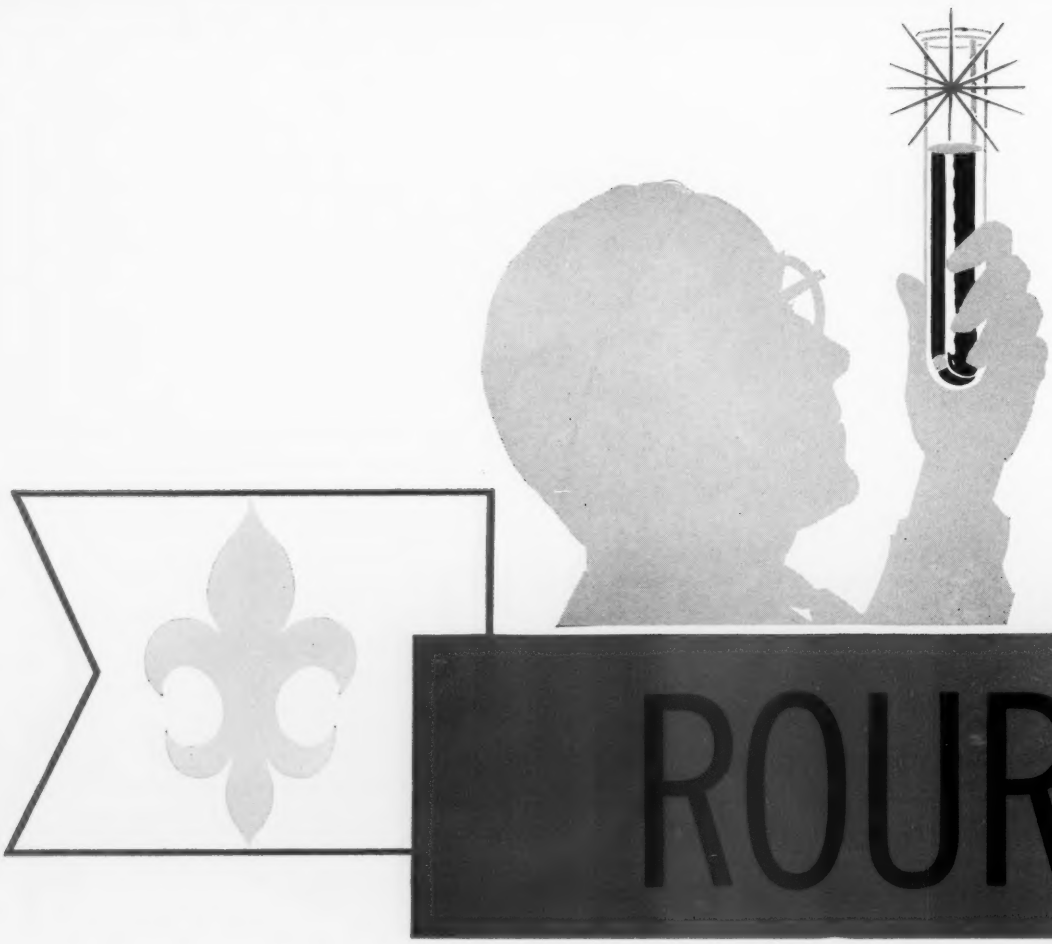

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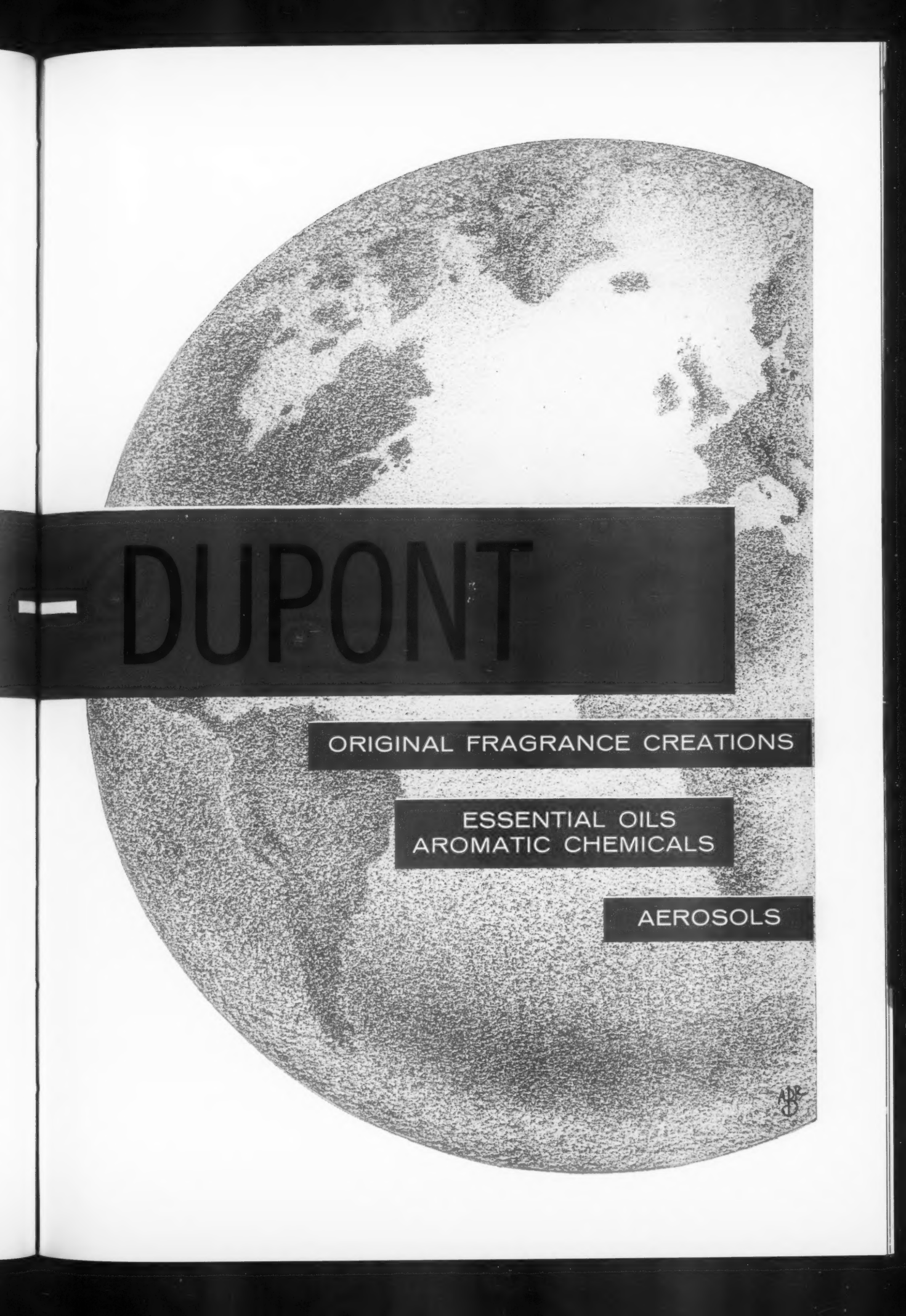
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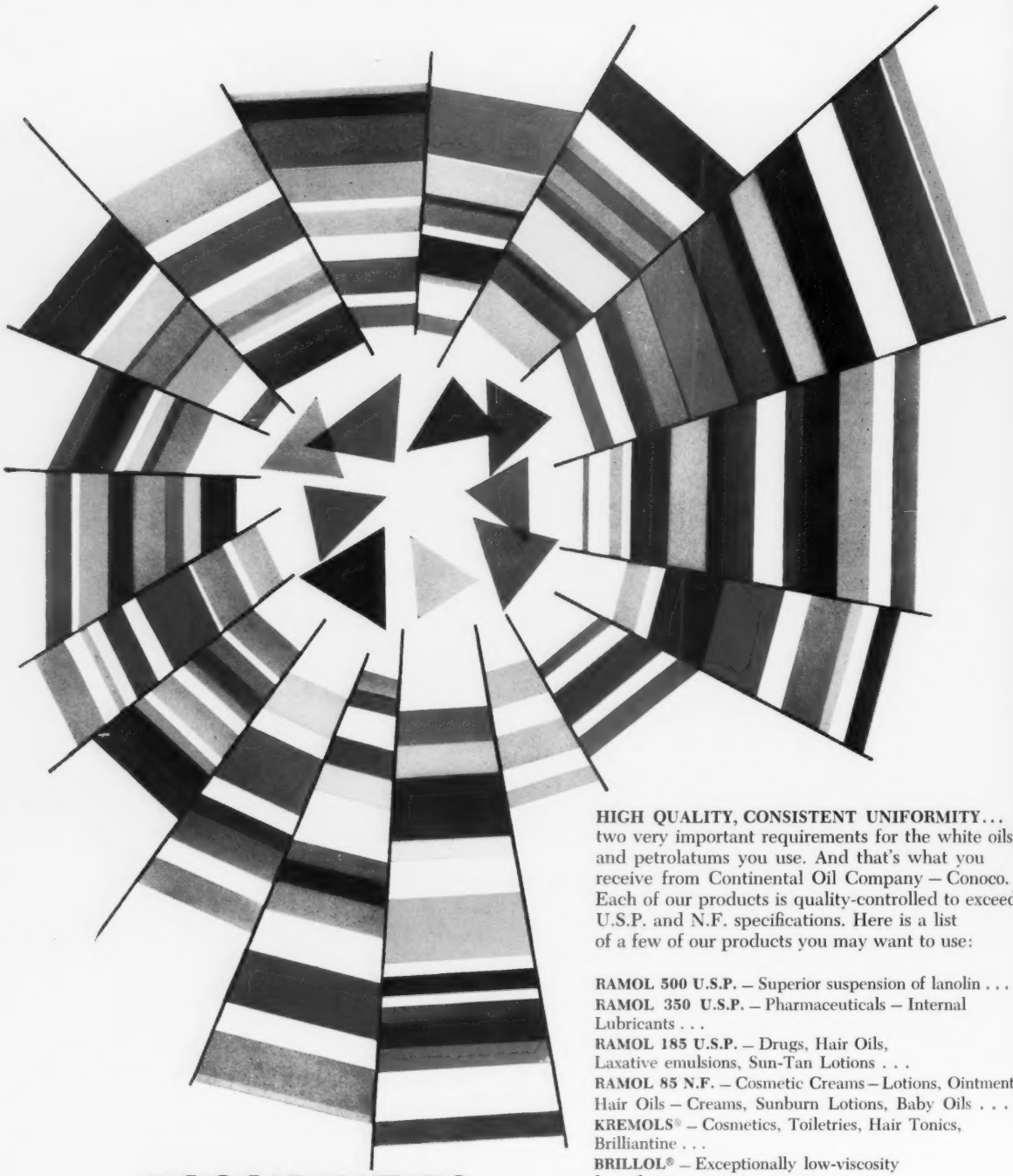

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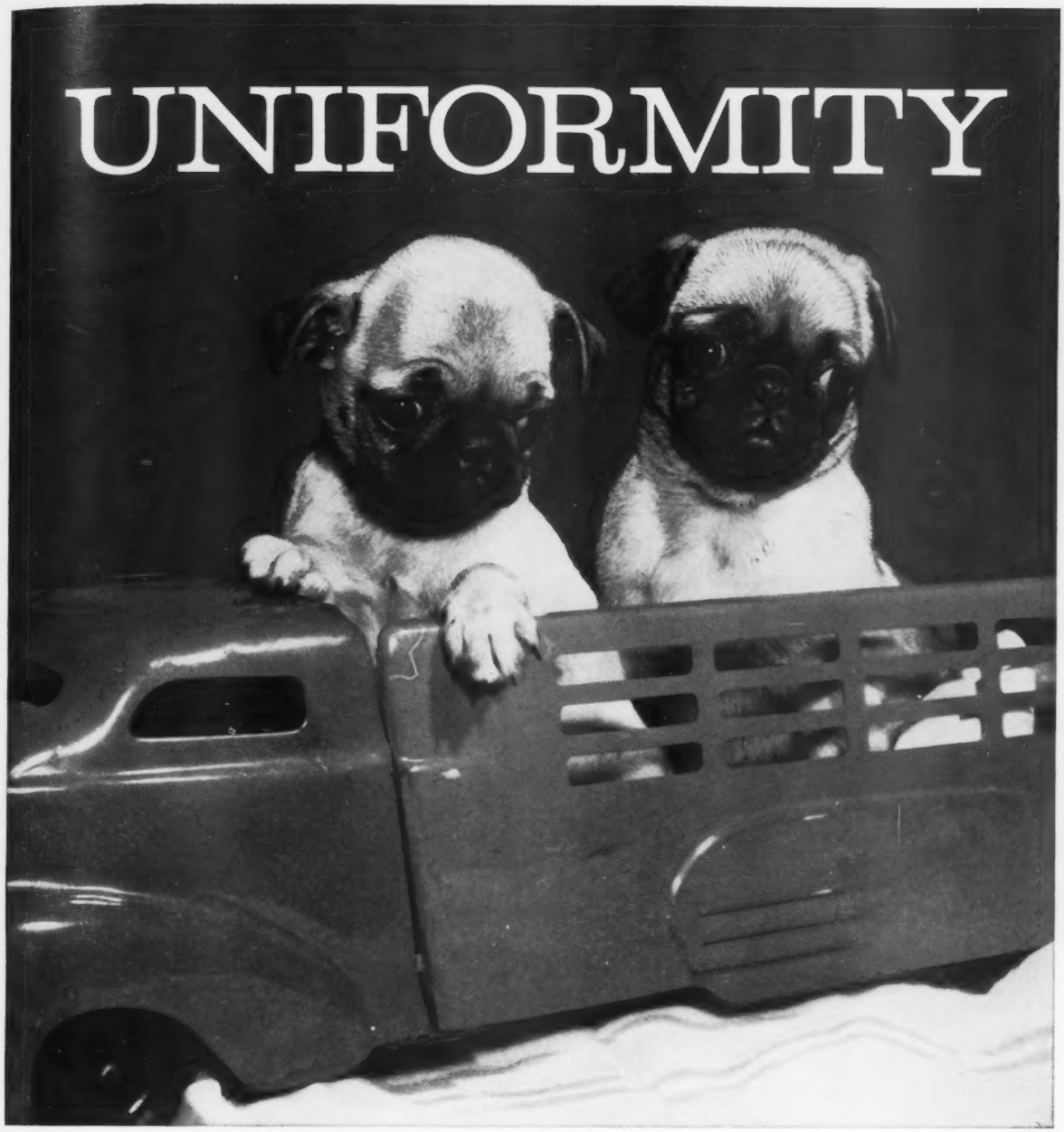

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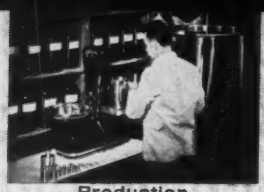

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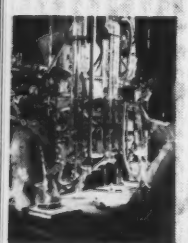

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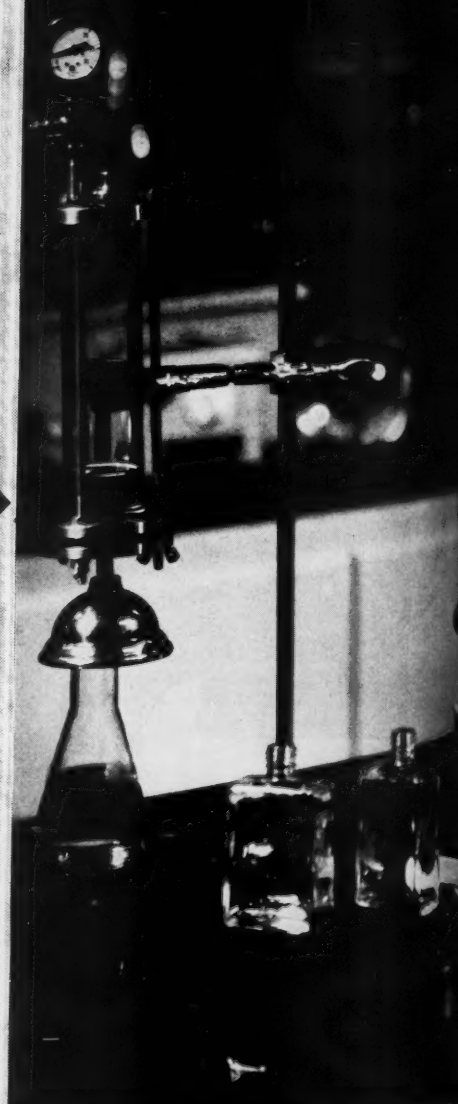

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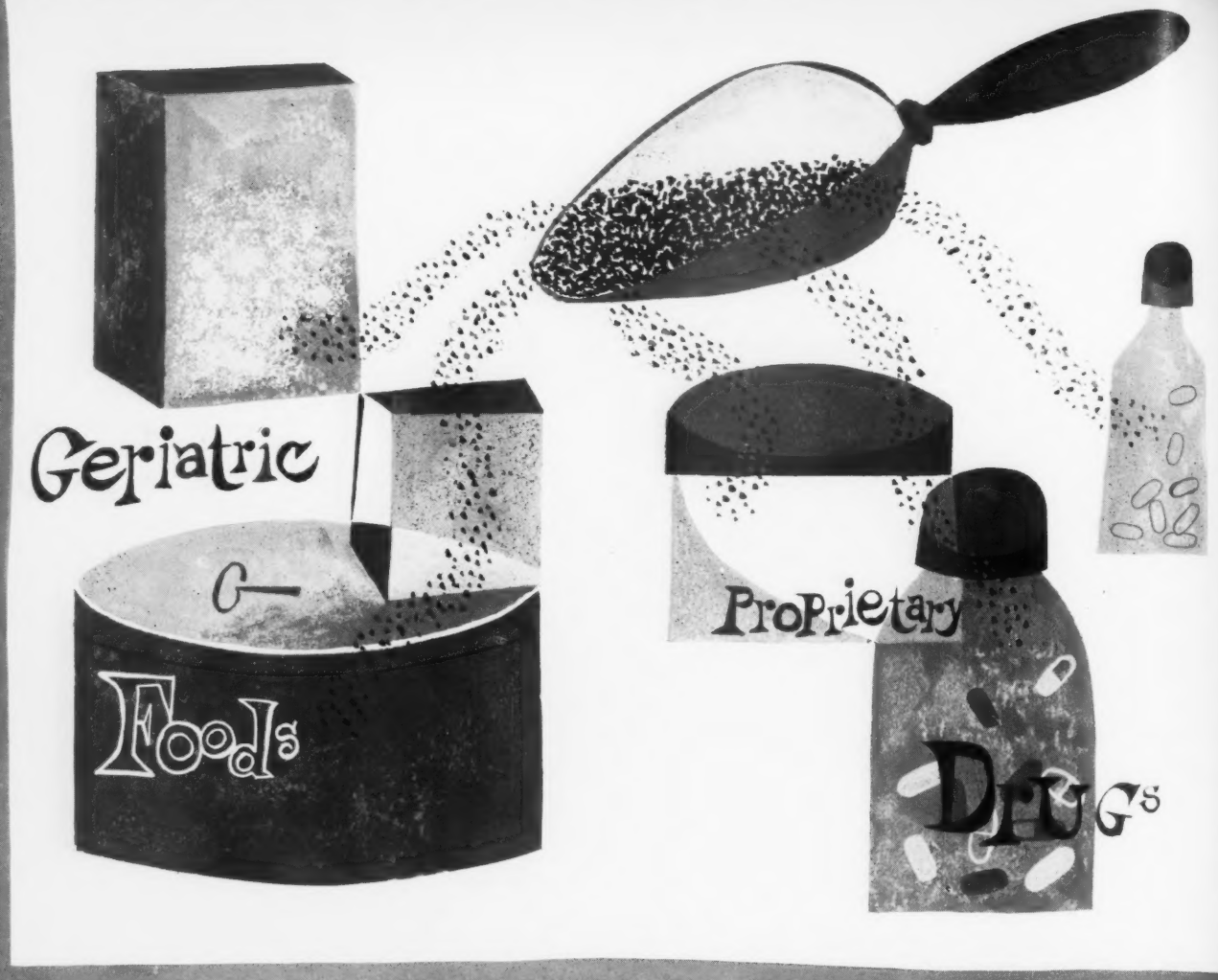

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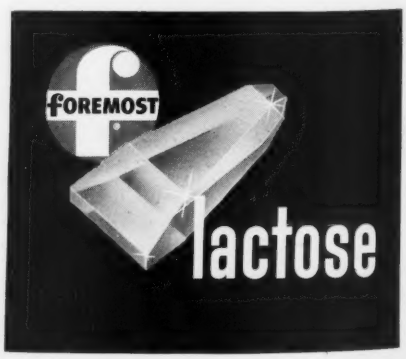

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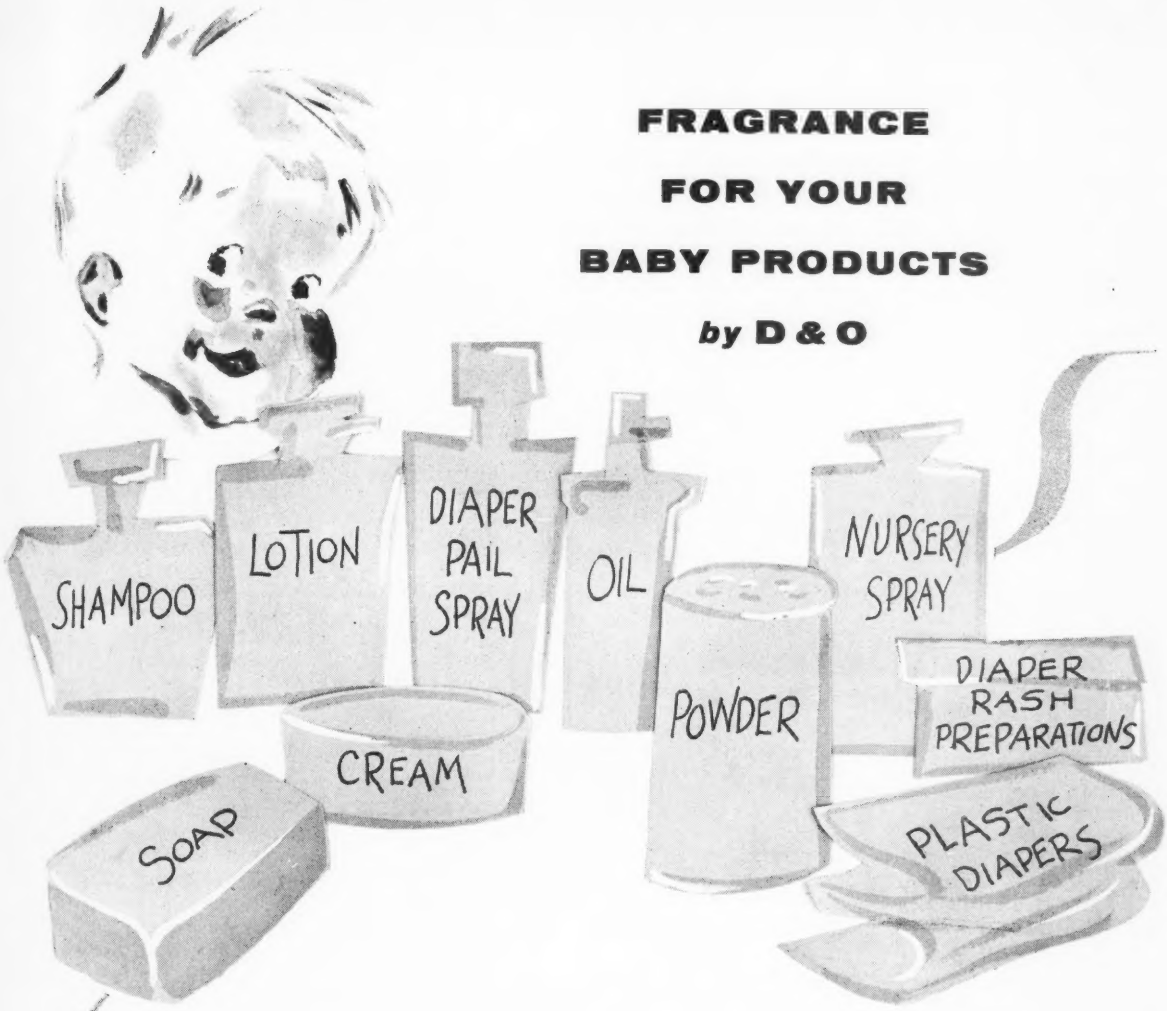

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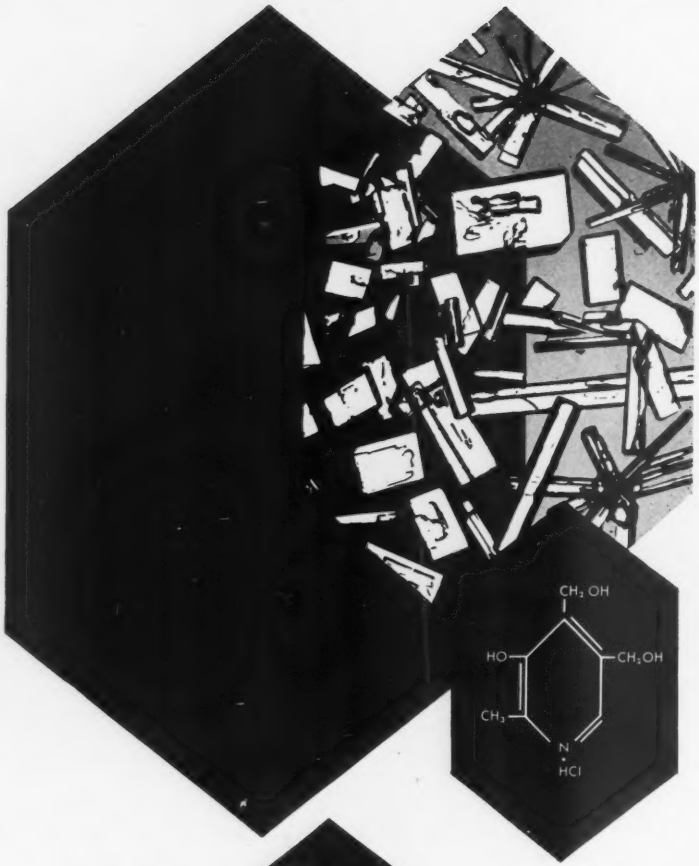

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Keeping Posted

TB and Drugs

While approximately 800,000 people in the United States have tuberculosis with 90,000 new cases being reported annually and 14,000 deaths occurring each year, the cost of caring for TB patients in VA hospitals dropped $38 million during the past three years. Dr. W. B. Tucker, Veterans' Administration director of tuberculosis service in Washington, D.C., says that due primarily to the discovery of drugs which can be used effectively for the disease, the time necessary for successful treatment has been reduced from two years to less than a year. Also TB patients can now return to productive employment soon after discharge from the hospital, while formerly he had to undergo prolonged home rest and slowly build up his strength.

Before the recent development of TB drugs, such as streptomycin and isonoazid, the relapse rate in TB was from 35 to 50 per cent, compared with less than 5 per cent today. Since the introduction of chemotherapy in the last ten years, the hospital death rate has been cut from more than five per cent to about one per cent. The U. S. Public Health Service reported in 1956 that TB is costing the United States approximately $725 million per year.

Lilly and Biologics

Eli Lilly and Company report that sales for the first six months of 1958 were off $12.9 million from $100.6 million for 1957 to $87.7 for 1958. Profits for the six months were off $6 million form $17.7 in 1957 to $11.7 in 1958. President Eugene Beesley says: "Sales in all major product lines except biologicals showed satisfying increases."

What this statement means is that biological sales declined by more than $12.9 million, and that the profit on biologicals declined by more than $6 million.

Ponds Sales

By revealing the loss in sales volume caused by the termination of the agreement for the sale of Vaseline products, the Colgate-Palmolive Company has inadvertently revealed the approximate 1957 volume of Ponds products. Colgate-Palmolive states that their sales for the first six months of 1958 reached a new high of $265,446,000, an increase of $10,572,000 over the preceding year, and not including any sales of Vaseline products which were sold by Colgate under contract during the first half of 1957. Excluding sales of these products, says Colgate, the increase in sales of company products for the first six months of 1958 was more than $20 million.

This means that during the first six months of 1957, Colgate sold approximately $10 million worth of Vaseline products, which means that the sales of these products for the entire year of 1957 were approximately $20 million. Since the total sales volume of Chesebrough-Ponds for 1957 was $55,496,000, it looks as though 1957 sales of Ponds products were somewhere in the neighborhood of $35 million.

Medical Research and Education

A report on Medical Research and Education by a group of consultants appointed by former Health, Education, and Welfare Secretary Marion B. Folsom has appeared in preliminary form. Appointed in August, 1957, the eighteen months life of the committee was cut half in view of Secretary Folsom's retirement. Six two-day meetings were held by the group.

The 117-page preliminary report emphasizes that U. S. medical research will continue to expand and advises that support be properly balanced between governmental and private sources. The consultants estimate that annual U. S. medical research expenditures may reach $1 billion by 1970, and suggest that not

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more than half of that sum come from government. According to them, philanthropy and industry should supply $500 million for medical research each year by 1970. They urge substantial expansion of teaching and training facilities, and insist that research cannot be expanded without an adequate supply of competent personnel. They recommend that:

"Base grants for research and training, distributed on the basis of professional judgments of the unique capacities and needs of each institution and not made to finance specific projects or programs, be provided to institutions.

"The National Institutes of Health support additional research in the medical and social and behavioral sciences directed towards the solutions of problems of extreme economic, social, or human significance.

"The National Institutes of Health support clinical research more adequately."

The consultants recommend the following policies:

"Maintenance of diversity of support as between public and private sources, and provision of funds from a number of Federal sources. It is important to avoid undue dependence upon any one source of funds.

"Provision of Federal support under terms and conditions which take account of the fact that medical education and research are inseparable in universities.

"Continuation of a rational Federal program of research support that attains and sustains a balance between aid for research, training of manpower, and construction of teaching-research facilities.

"Expansion of Federal aid to medical research primarily through support of activities in non-Federal laboratories. Federal laboratories should be a decreasing proportion of the total Federal activities in support of medical research."

Says the report:

"The Congress has directed that certain specific research be undertaken. This tendency to earmark funds, which cannot prove constructive over the long run, has been somewhat fostered by the fact that the whole structure of the National Institutes of Health has been built around disease categories. Some of the directives are in sufficiently general terms, or contain qualifications that provide adequate leeway to administrators. Other directives are orders to pursue research that is already in progress. Some of the directives stimulate research and do so in a way that has proved to be useful. For example, appropriations committees of both houses of Congress have repeatedly admonished the National Institutes of Health to ensure that basic research be adequately supported. . .

"Provision of research grant funds through Institutes named after diseases—the so-called categorical approach—has been called a defect in the system. In the opinion of the Consultants, this is not inevitably the case. The system is administered to permit support of fundamental as well as applied research. The categories in the aggregate are all-inclusive. The system does not lead to overemphasis upon applied research. The independent investigator is not required to 'angle' or 'slant' his research. These aspects of the categorical system are not fully understood. . .

"Large-scale development research, designed to find new drugs (as in the case of the cancer chemotherapy program administered by the National Cancer Institute) to assess known agents (as in the psychopharmacology program administered by the National Institute of Mental Health) or to determine the causes of disease (as in studies of the perinatal period administered by the National Institute of Neurological Diseases and Blindness), has expanded rapidly with the aid of NIH research grant and contract funds. Such programs generate complex administrative problems, and they raise basic policy questions of the roles of government, universities, and industry.

"The Consultants recommend that:

"Before extension of such programs above the level in the current fiscal year, intensive attention be paid to thorough consideration of the basic policy questions, to care in planning, to realistic assessment of the present state of studies of this kind, and to consideration of the effect on all medical research of absorption of resources—particularly manpower—by such programs.

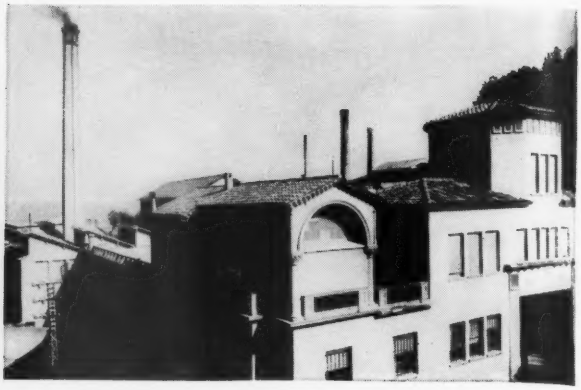
"As a principle, the primary resources for development and production of new drugs be the investment of private industry; and such drugs as may result from intramural research at NIH be a byproduct of other studies and not the outcome of an NIH intramural drug development program. . ."

The chairman of the group of consultants is Dr. Stanhope Bayne-Jones, former Dean of Medicine at Yale, and the executive secretary is Dr. Charles V. Kidd, chief of the office of research planning of N.I.H. Other members are: George P. Berry, M.D., Dean of Harvard Medical School; Thomas P. Carney, Ph.D., Eli Lilly and Company; Lowell T. Coggeshall, M.D., Dean, Division of Biological Sciences, University of Chicago; Fred C. Cole, Ph.D. Academic Vice-president, Tulane University; Samuel Lenher, Ph.D., E.I. du Pont de Nemours & Co.; Irvine H. Page, M.D., Director of Research, Cleveland Clinic Foundation; Robert C. Swain, Ph.D., American Cyanamid Company; Stafford L. Warren, M.D., Dean of Medicine, University of California; and James E. Webb, Republic Supply Company.

Polio Foundation Expands

The National Foundation for Infantile Paralysis has shortened its name to the National Foundation, but has broadened its activities to include, in addition to polio, research and professional education on virus diseases, arthritis, birth defects, and central nervous system disorders, as well as patient care for children through 18 years of age afflicted with arthritis and birth defects.

Foundation president, Basil O'Connor said that the foundation's long-range plans do not limit it to these



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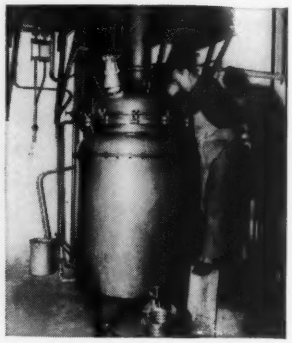

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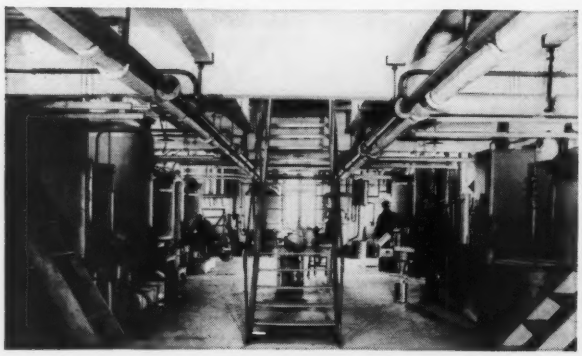

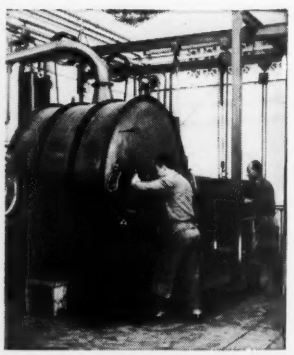

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specific fields. Rather, he said, the group will be a major force in medical research, patient care, and professional education. Mr. O'Connor said that the foundation could "intelligently spend $60 million in the first year of expanded operation, but this figure is not by any means the firm goal of the March of Dimes for 1959. The foundation collected $35.4 million in its 1958 drive.

Since the foundation was founded in 1938, it has collected $490 million and has committed virtually all of it: Research $34 million; Patient Care $316 million; Education $35 million; Polio Prevention $36 million; Ancilary Services $39 million; Administration of national organization and its chapters, which now number 3,100, $21 million. There is a balance on hand of $2 million, and the chapters owe about $6 million. The cost of collection is 10 to 12 per cent.

Freedom to follow research clues whereever they may lead will be combined with necessary limitations on patient aid in the beginning. The limitations result from the enormity of the problem: At least 11 million people have arthritis and rheumatism; 250,000 children are born with significant birth defects each year (excluding birth injuries), and an estimated 150,000 persons who have had paralytic polio will require some assistance in the years ahead. It is hoped to work with some 16,000 who seek treatment of the 30,000 annually affected with rheumatoid arthritis, and with some 8,000 patients annually with birth defects of the central nervous system that are treatable.

"Our objective in patient care is to continue the polio job until it is finished," said Mr. O'Connor. "We have a moral obligation to do this and the American people expect us to recognize this responsibility. We shall begin patient aid in arthritis and birth defects, first, where it will do the most good and, second, on a scale commensurate with the public's willingness to finance it."

New Drugs and Company Welfare

The importance of efficacous new drug products to the welfare of the companies discovering and marketing them is indicated in several financial reports for the first half of this year. For example, Dr. W. G. Malcolm, president of the American Cyanamid Company, remarked on the fact that the sales of his company were only off slightly from a record volume of $259,100,000 in 1957 to $257,400,000, that operating results "were affected by the general business recession and sales of many products and some product groups declined. The aggregate reduction in sales, however, was virtually offset by a number of new products introduced since the forepart of last year, including Aristocort triamcinolone, a new steroid compound for the treatment of rheumatoid arthritis, allergies and certain skin disorders; triple superphosphate, a high concentrate fertilizer material, and Pathibamate, a new agent for the treatment of gastrointestinal ulcers." Note that two of the three products responsible for holding up this company's sales are drug products.

A similar situation obtains in Merck & Co. which shows an increase in sales to $101,492,000 for the first six months of 1958, from $91,304,000 for the first half of 1957. Merck president John T. Connor said that improved 1958 results were the wide medical acceptance of Diuril, a new pharmaceutical specialty used in treating diseases of the circulatory system and other serious conditions, and increased sales of coccidiostats (product for control of the poultry disease coccidiosis. "However, added Mr. Connor, "we continue to encounter weakening of prices or lessening of demand, or both, for many important products. These soft spots have adversely affected sales and earning of some vitamins, steroid hormones, antibiotics, and industrial chemicals." In this case, due to drug products, both sales and earnings have advanced in an otherwise weak market.

On the other hand, Schering Corporation's 3 per cent decline in sales from a record of $38,996,000 for the first half of 1957, to $37,837,000 in the first half of 1958, is said to reflect growing competition in the corticosteroid market. Schering president, Francis C. Brown said that "while sales of the Company's anti-inflammatory 'Meti' drugs had been affected by the introduction of two competitive products early in 1958, Schering retained a major portion of the market and sales of other products showed continued growth."

The decline of 13 per cent in Schering earnings is said to reflect increased sales and advertising expenses, expanded research activities, changes in royalty accruals, and foreign exchange losses in Chile and Colombia.

Carter v. Colgate

In a 42-page decision, Chief Judge Thomsen of the U. S. District Court in Baltimore held that Colgate-Palmolive violated a previously entered injunction by causing the sale of 1,600,000 cans of its Freon type pressurized shaving creams and should pay triple damages and attorney fees to Carter Products, holders of the patent covered in the injunction and makers of Rise. The Court also held that Colgate-Palmolive's present shaving cream is the equivalent of Carter's patented Rise, but did not find infringement because of a position which the Court found the patentees had taken in obtaining their patent in the Patent Office.

Carter attorneys are studying the opinion to determine what steps should be taken by appeal or otherwise with respect to a likelihood of infringement by Colgate-Palmolive's present products.

Butazolidine and Preludin

Noting that the imports of Butazolidine totaled 25,680 pounds, we converted this to 11,673 kilograms, or 11,673,000,000 milligrams. This would make 116,730,-

000 100 mg. tablets, or 1,167,300 bottles of 100 tablets each. Since the cost to the wholesaler of each bottle is in the neighborhood of $3.68, it would appear that the total business in the item in this country is close to $4,000,000 per year.

Noting also that imports of another Giegy drug product, Preludin, totaled 6,612 pounds, or 3,005 Kilograms in 1957, we converted this to determine that it would make 120,200,000 25-mg. tablets or 1,202,000 bottles of 100 tablets. Since these bottles sell to the wholesaler for about $3.60 each, we find that Giegy also has a total business in this item in this country of somewhere in the vicinity of $4,000,000.

Glenbrook Laboratories

Glenbrook Laboratories is the new name given to the National Brands Division of Sterling Drug, Inc. The Glenbrook name is taken from Glenbrook, Connecticut, the site of the plant first opened in 1856 by Chas. H. Phillips who originated Phillips' Milk of Magnesia, the oldest name in the organization. Phillips' Milk of Magnesia is still made at the Glenbrook plant, as well as at a plant in Gulfport, Mississippi. The renamed division was organized in 1956 to coordinate the sales and promotional operations of the Bayer, Phillips, and Centaur-Caldwell divisions of Sterling. Its principal products, in addition to Phillip's Milk of Magnesia, are Bayer Aspirin, Fizrin Instant Seltzer, Z.B.T. Baby Powder, Dr. Lyon's Tooth Powder, and Fletcher's Castoria.

MCA Urges Additive Bill Enactment

The manufacturing Chemists Association has urged Congress to enact HR 13254, which is an amendment to the Food, Drug, and Cosmetic Act for the control of food additives. The bill has been approved by the Health and Science Subcommittee of the House Committee on Interstate and Foreign Commerce. Representative John Bell Williams (D. Miss.) is chairman of the subcommittee, and Representative Oren Harris (D. Ark.) is chairman of the full committee.

In writing to Chairman Oren, General John E. Hull, MCA president, that while:

"The new bill does not conform to a number of recommendations made by our witnesses before your Committee, which we continue to believe would make possible the most workable law and one which would afford no less protection to the public health than HR 13254. . . . We favor the immediate enactment of HR 13254 . . . for three principal reasons. First, because it is in the public interest to clarify the existing procedures at the earliest possible time. Second, because several years are needed to accomplish the pretesting of food additives, it is important that the procedures be settled in order that the scientific development of further improvement in the Nation's food may progress without uncertainty as to future legal requirements. Third, because the interest being manifested by state and local health officials could readily lead to greater consideration of state and municipal regulation of food additives, which recently occurred in Utah, New York, and in New York City. The enactment of state or municipal legislation on this subject could take a variety of forms and provide for a variety of sometimes conflicting procedures. The enactment of a Federal law at this time will set a pattern for state and municipal legislation just as the present Food, Drug, and Cosmetic Act has set a pattern for state food and drug acts in the past."

N.I.H. Appropriations

A total of $294 millions was voted for the N.I.H. by Congress, or 75 per cent more than the House had proposed. Rounded off figures for the various institutes, in millions of dollars, are general research 29, cancer 75, mental health 52, heart disease 45.6, dental research 7.4, arthritis 31, allergy and infectious diseases 24, and neurology and blindness 29. The Hill-Burton hospital construction program is to receive $186 million in contrast to $121 proposed by the House. Diagnostic-treatment centers and chronic disease hospitals were cut from the Senate's $20 million to $7.5 million each, but Senate figures were accepted for rehabilitation centers and nursing homes, $10 million each. For a national library of medicine $6.9 million was voted, as well as $9.6 million for an office building at N.I.H.

Hospital Formulary

The first American hospital formulary, a book of drugs and doses designed to promote better patient care, is to be available in September. It is being prepared by Assistant Professor of Pharmacy Don E. Francke, chief pharmacist at the University of Michigan Medical Center. Publication and distribution is being arranged by the American Society of Hospital Pharmacists.

Until now, each hospital has prepared its own formulary, or managed to get along without one. The new work is designed to provide a quick reference for physicians, nurses, and pharmacists regarding dosage schedules, possible side effects and unusual procedures necessary in administering today's complex pharmaceuticals. The book will also be helpful in selecting the best drug and dosage for a patient. The A.S.H.P. Hospital Formulary, as it will be called, will be in loose-leaf form to provide for future additions and deletions of specific drugs.

Pfizer Buys Vigo Plant

Chas. Pfizer & Co. has purchased from the Federal Government the Vigo plant seven miles south of Terre Haute, which the company has operated under lease since 1947. Pfizer has used these facilities, part of a World War II Army ordnance installation, for production of antibiotics and animal feed supplements. Recently, Pfizer reconstructed a number of buildings for the manufacture of vaccines. Included

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in the purchase are fermentation facilities utilized by Pfizer for manufacture of streptomycin, Terramycin, and other antibiotics. The plant employs approximately 500 persons. Another Pfizer installation, the 700-acre Agricultural Research and Development Center, largest privately-owned research facility of its kind in the world, is located on private property about a mile from the plant.

In addition to the Vigo plant, Pfizer has plants in Brooklyn, N. Y., Groton, Conn., Greensboro, N. C., and 14 foreign countries.

F.D.A. Expansion Approved

With reference to the Food and Drug Administration, the Group of Consultants to HEW Secretary Folsom, said:

"The Consultants accept the conclusions of the Citizens Advisory Committee, relevant to research and training, supplemented by discussions with the staff of the organization and by the fairly extensive personal experience of some of the Consultants in working with the Administration, as a sound guide to the development of the Food and Drug Administration.

"The Consultants are of the opinion that a vigorous research effort is critically important to the effective performance of the statutory responsibilities of the FDA. Clinical investigations, research on improved analytical and testing methods, toxicological research, and observation of the effects of antibiotics over long periods of time must be carried on with well qualified personnel, having adequate equipment, funds and facilities at their disposal.

"FDA finds it difficult to compete not only with industrial salaries, but with salaries paid by some other governmental agencies."

Lilly Digest for 1957

The 26th annual edition of the Lilly Digest, covering the operations of 2,142 retail pharmacies throughout the country for 1957, shows that the sales increase was 12.3 percent over 1956 for the greatest increase ever reported. Sales in 1957 were 35 percent over those of 1952. Gross margin, proprietor's salary, and net profit also were at record levels. Prescription income and the number of prescriptions filled broke all previous records, but prescription department inventory as a percentage of prescription receipts was at record-low level. Income from numbered prescriptions was nearly two and one-half times that of 1950. However, the Report shows a percentage increase in total inventory greater than the percentage increase in sales even though there was a continued decline in the proportion of prescription inventory to prescription sales. As a percentage of sales, proprietor's salary, employees' wages, and miscellaneous operating costs again moved upward to produce a peak for total expenses. The result was a decline in net profit percentage.

There is a decreasing number of the Lilly Digest pharmacies reporting sales of less than $50,000 per year. Among the 2,142 pharmacies represented, only 11 per cent had sales of less than $50,000, while ten years ago, 35 per cent were so classified. At the other end of the scale, 27 per cent of these pharmacies had sales in excess of $150,000 in 1957, as compared with 6 per cent in 1947.

The Digest points out that total income in stores with sales in the neighborhood of $25,000 per year approximates $4,400, or about $85 per week. Thus, it may be assumed that a pharmacy of this sales size offers no more (and in most instances, less) income potential than full-time employment in a retail pharmacy. Not until sales reach the $60,000-per-year level can the proprietor of a full-line pharmacy expect an annual income of $10,000.

Unfortunately, says the Digest, total income in the average pharmacy does not increase in direct proportion to increases in sales. Total income among the lowest sales-volume group was 17.6 per cent of sales as compared 10.6 in the highest. The difference lies principally in the larger proportion of sales withdrawn for salary by proprietors of small-volume stores.

As a percentage of sales, operating costs remain fairly constant no matter what the sales volume may be. Average total expenses as a percentage of sales were identical in high and low sales-volume groups. Operating costs among the ten groups ranged from 26.6 to 30.7 per cent of sales.

The growth of prescription business during 1957 was assisted by a record percentage of refills, says the Digest. Refills in 1957 established a record of 45.7 per cent of the total number of prescriptions filled. It might be assumed that prescription refill business has actually been stimulated by the Durham-Humphrey Amendment to the Federal Food, Drug, and Cosmetic Act, which was designed to prevent refills. As a result of this amendment a great many prescriptions now carry specific refill instructions which the patients feel obligated to follow. Refills have also become more important because of recent medical advances, particularly in the field of geriatrics and in the treatment of chronic-type diseases.

The increase in prescription sales in the Digest stores was 22.4 percent, compared with a 14.4 percent for sales of other items. Of the 1,862 stores reporting prescription department data for 1957, the average increase in prescription income in 1957 over 1956 was $7,047. The average number of prescriptions filled rose 1,517, and the average price advanced from $2.62 to $2.85. Therefore, the increase in the number of prescriptions filled accounted for $3,945, and the rise in the average prescription price accounted for $3,102 of the prescription income gain. A total of 25,140,724 prescriptions was involved in the 1957 summary of these 1,862 prescription departments.

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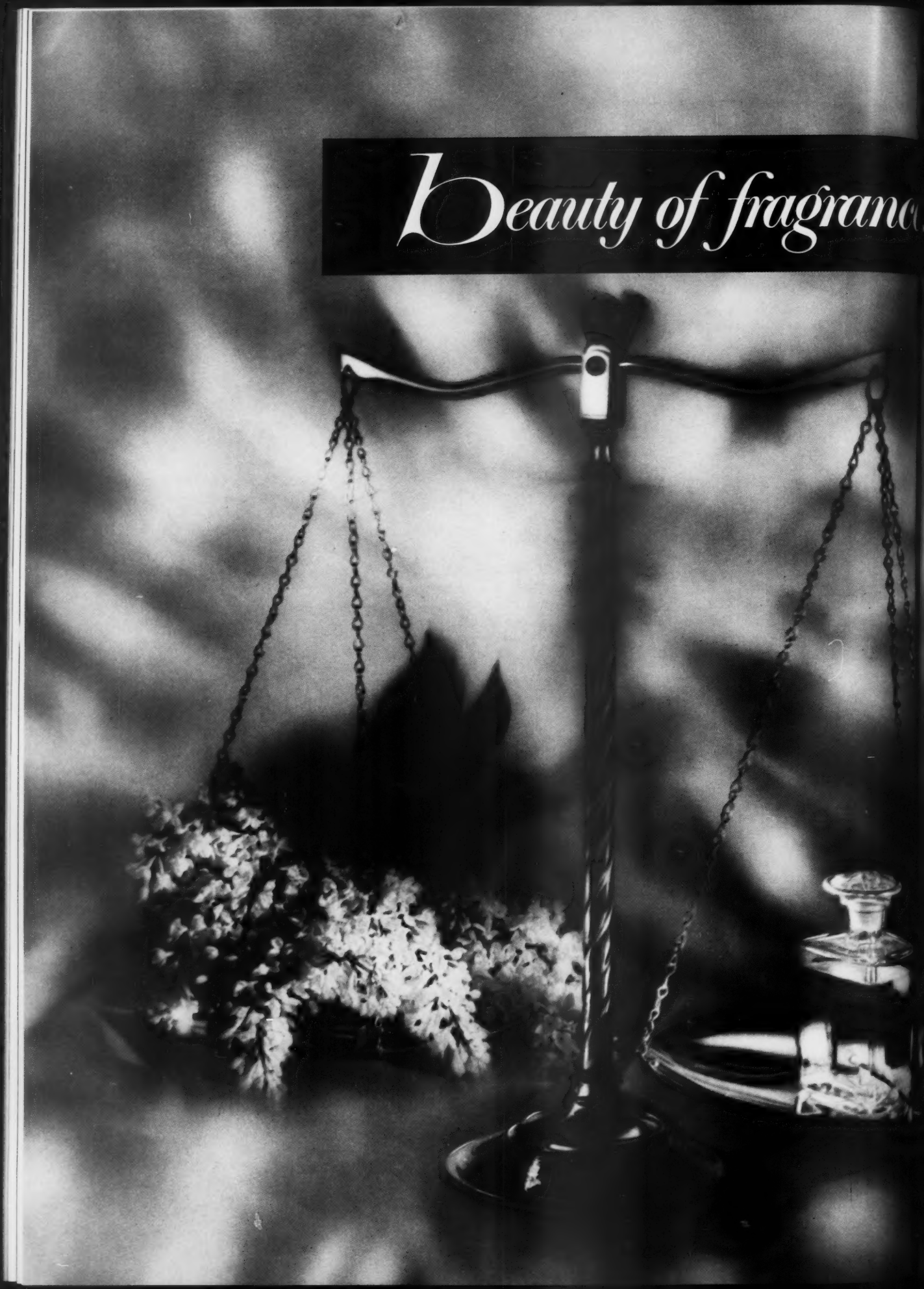
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— Goodman and Gilman, THE PHARMACOLOGICAL BASIS OF THERAPEUTICS, Second Edition (Page 827). Published by The Macmillan Company (1955).

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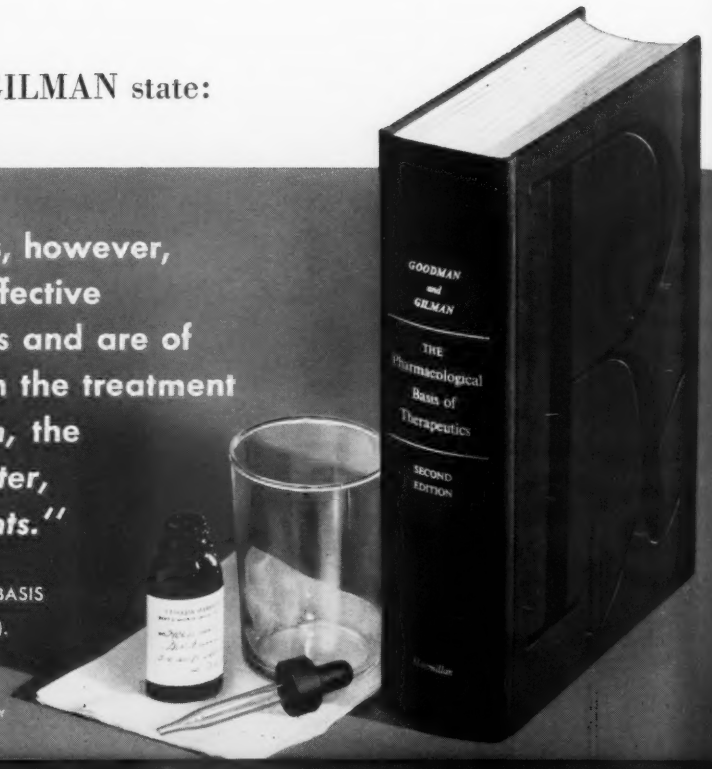

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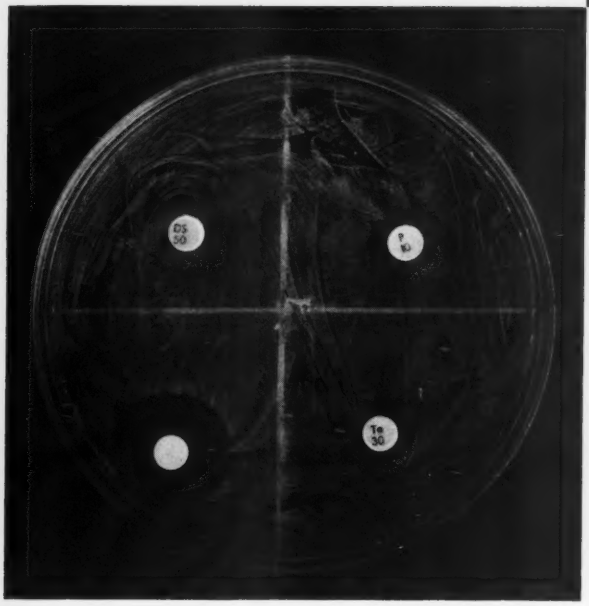
KANAMYCIN

BY JOSEPH KALISH, PH. D.



A new antibiotic, kanamycin, was the subject of a two-day symposium held at the Barbizon-Plaza Hotel in New York under the joint sponsorship of The New York Academy of Sciences and Bristol Laboratories. The product is being sold by Bristol under the trade name "Kantrex."

Kanamycin comes from *Streptomyces kanamyceticus*, a culture first isolated by Dr. Hamao Umezawa and his colleagues in Japan. It is valuable as a bactericidal antibiotic in the treatment of Staphylococcal and some other infections resistant to usual antibiotics; it has some degree of effectiveness against tubercle bacilli that have become resistant to streptomycin and isoniazid; it is very effective on oral administration in sterilizing the bowel before intestinal surgery and in the treatment of Salmonellosis and Bacillary Dysentery; intramuscular administration is effective against a number of otherwise stubborn chronic urinary tract infections and intraperitoneal instillation, in conjunction with wide-spectrum antibiotics, controlled and prevented peritonitis.

The usefulness of kanamycin as a panacea is limited, however, by a number of factors: systemic action is possible only on intramuscular (and intravenous) injection, since the drug is poorly absorbed on oral administration; injection is painful, probably because of the hypertonicity of the solution; there are some indications of nephrotoxicity; large and long-continued doses lead to eighth nerve toxicity and vestibular disturbances as with streptomycin; bacteria develop resistance to the new antibiotic.

One of the clinical papers indicated that the simultaneous use of procaine reduced irritation at the injection site, as was the case with penicillin. It is not impossible that dosage forms may be developed to provide longer action or repository effect to reduce the frequency of dosage and perhaps reduce the overall amount required for treatment. No work has yet been presented concerning the possibility of active and less-toxic derivatives as in tetracycline and streptomycin itself. Meanwhile, this useful antibacterial, at least in its earlier clinical stages, will require watchfulness with respect to its toxicity and the development of resistance.

Kanamycin was first obtained as its amorphous hydrochloride and sulfate according to H. Umezawa of the University of Tokyo. However, an active effluent of carbon chromatography which was pH about 8.0 gave a crystalline sulfate when the same volume of methanol was added. The crystalline sulfate was confirmed to be the monosulfate of kanamycin, $C_{18}H_{36}O_{11}N_4.H_2SO_4.H_2O$.

It exhibited therapeutic effects on infection of pneumococci or typhoid bacilli in mice. Results of acute and chronic toxicity test with mice, rats, cats and dogs suggested the safety for the clinical studies. The first clinical studies were made by Doctor Ichikawa. Doctor Yanagisawa confirmed its effect on experimental tuberculosis in mice and guinea pigs and clinical studies on pulmonary tuberculosis were be-

Examining model of kanamycin held by Dr. I. R. Hooper, chemical research department, Bristol Laboratories, are (left to right): Dr. Yahisa Kotake, chief, research and development section, the Meiji Seika group; Dr. Toluji Ichikawa, director, Tokyo University Hospital; Dr. Hamao Umezawa, director, antibiotic division, National Institute of Health, Tokyo; Dr. Amel R. Menotti, Bristol research director.

gun by Doctor Donomae.

Kanamycin studied by M. J. Cron et al. of Bristol Laboratories, is a water-soluble basic antibiotic with hydroxyl and primary amine fuctional groups. Kanamycin has been additionally characterized as Schiff base derivatives, as the tetra-N-acetate and as a polyacetate. It gives positive Molisch, ninhydrin, and Elson-Morgan tests and is strongly dextrorotatory. Kanamycin base and sulfate are soluble in water and insoluble in non-polar organic solvents.

A related antibiotic, kanamycin B, has been isolated from kanamycin fermentations and characterized.

Acid hydrolysis of kanamycin yields 2-deoxystreptamine, which has also been obtained from neomycin A (neamine), and two amino sugars. The first amino sugar to be studied was shown to be 6-amino-6-deoxy-D-glucose.

The other hexosamine, designated kanosamine, has been shown to be a 3-amino-D-aldohexopyranose. Partial hydrolysis studies on kanamycin have shown that both hexosamines are linked glycosidically to deoxystreptamine and periodate oxidation studies on tetra-N-acetylkanamycin and kanamycin base have proven that these linkages are on the 4 and 6 positions of deoxystreptamine.

Microbiological studies of Kanamycin were made by A. Gourevitch et al. It is active against a wide variety of Gram-positive, Gram-negative, and acid-fast organisms. The range of its *in vitro* activity includes *Staphylococcus*, *Bacillus*, *Vibrio*, *Salmonella*, *Shigella*, *Mycobacterium*, and some strains of *Proteus* and *Pseudomonas*. On the other hand, it is relatively inactive against *Streptococcus*, *Diplococcus*, and *Clostridium*.

Kanamycin is very active against clinical strains of *Staphylococcus* resistant to the commonly used antibiotics, penicillin, streptomycin, the tetracyclines, erythromycin, chloramphenicol, and novobiocin. Its action is bactericidal.

In vitro, using serial transfer techniques, *Staphylococcus aureus* and *Escherichia coil* develop resistance to kanamycin in a slow, step-wise fashion in contrast to the rapid development of resistance seen with streptomycin.

Such strains show complete cross resistance to neomycin and partial cross resistance to streptomycin.

Studies carried out with combinations of kanamycin and penicillin indicate that there is no interference with each other's action and that the two antibiotics are consequently compatible.

D. E. Tisch et al. studied the toxicity of kanamycin. The LD_{50} of kanamycin sulfate in mice is 316.3 $\pm$ 24.4 mg./kg. (intravenous), 1648 $\pm$ 54.4 mg./kg. (subcutaneous), 1679 $\pm$ 186.4 mg./kg. (intraperitoneal), and >10,000 mg./kg. (oral).

Subacute toxicity studies in mice indicate kanamycin sulfate is slightly less toxic than streptomycin sulfate and considerably less toxic than neomycin sulfate. Kanamycin sulfate was non-toxic to growing rats at daily subcutaneous doses of 200 mg./kg. during six months and at oral doses of 400 mg./kg. during one month. Dihydrostreptomycin sulfate subcutaneously in rats had an earlier and more pronounced effect on auditory perception than did kanamycin sulfate at the same dose.

Daily subcutaneous injections (100 mg./kg.) of streptomycin sulfate into cats uniformly caused loss of equilibrium and righting reflex in two to six weeks. This same dose of kanamycin produced these effects in only one out of five cats during six months of treatment. Higher doses of streptomycin sulfate or kanamycin sulfate (200 mg./kg.) caused changes in equilibrium and righting reflex with the changes occurring earlier with streptomycin.

Dogs tolerated daily intramuscular doses of 100 mg./kg. of kanamycin sulfate for eight months with no sign of toxicity. Post-mortem examination of dogs sacrificed after six months did not show any pathology either grossly or microscopically. Higher doses (200 mg./kg. and greater) produced evidence of renal toxicity. Oral doses as high as 1000 mg./kg./day have had no ill effects.

Kanamycin is rapidly absorbed following intramuscular administration into animals, producing very high blood levels which decrease rapidly during six to eight hours. It is poorly absorbed following oral administration. Following intramuscular administration to dogs kanamycin appeared in the spinal fluid and bile. Over 50 per cent of a single dose was excreted in the urine during twenty-four hours. Kanamycin sulfate produced no significant electrocardiac changes or pharmacodynamic effects in intravenous doses up to 100 mg./kg. in anesthetized dogs.

To form a basis for the interpretation of blood concentrations obtained in man, bacteriostatic and bactericidal concentrations of kanamycin were determined by Henry Welch et al. for 57 cultures of gram-positive and gram-negative organisms. Kanamycin in concentrations of 2.0 to 7.8 mcg./ml. were bactericidal to ten clinical isolates of *Staphylococcus aureus* all resistant to penicillin. Six of the ten *Salmonella* cultures were sensitive to from 15.6 to 31.2 mcg./ml. (bactericidal). Following single intramuscular injections of kanamycin solution in three groups of ten normal adult men the following average peak concentrations were obtained from various doses: 12.2 mcg./ml. (1 hour after 0.25 gm. dose), 22,2 mcg./ml. (1 hour after 0.5 gm. dose), and 31. 4 mcg./ml. (2 hours after 1 gm. dose).

In twenty-four hours 73.1 per cent of the 0.25 gm. dose had been excreted in the urine, as had 64.1 per cent of the 0.5 gm. dose, and 51.7 per cent of the 1 gm. dose.

Kanamycin according to G. A. Hunt and A. J. Moses is effective in the protection of mice against an otherwise overwhelming infection of *K. pneumoniae*, *D. pneumoniae*, *Proteus vulgaris*, and *Staph. aureus*. It does not protect against virulent strains of *Streptococcus hemolyticus* in mice. In general the curative action of the antibiotic may be predicted by the *in vitro* sensitivity of the organism for the antibiotic and the antibiotic blood level obtained in mice one to four hours following intramuscular injection.

Tests carried out using an overwhelming intravenous challenge of a staphylococcus resistant to penicillin, streptomycin, tetracycline, and erythromycin showed that kanamycin was effective where the other antibiotics were not.

Comparative observation of the therapeutic effects of kanamycin, streptomycin and isoniazid was made by K. Yanagisawa by the administration in 20 mg. daily dose for 15 weeks against guinea pigs infected subcutaneously with virulent human tubercle bacilli six weeks previously. The result was that each of those three drugs healed established tuberculosis almost completely.

Guinea pigs were infected intracerebrally with virulent human tubercle bacilli. Immediately before or after the onset of paralysis of the hind legs, treatment was started with kanamycin, streptomycin or isoniazid in 20 to 50 mg. daily dose. Streptomycin was found more effective than isoniazid and kanamycin.

Guinea pigs were infected intravenously with one of three drug-resistant strains and the day following infection drug administration was begun. The result was that kanamycin was active against experimental tuberculosis infection by any such drug-fast tubercle bacilli.

A kanamycin-resistant strain of tubercle bacilli was isolated in a single step on Kirchner agar medium containing kanamycin. This strain was further purified and inoculated into guinea pigs. Then the animals were treated with kanamycin, streptomycin or isoniazid. The result indicated that kanamycin-resistant tubercle bacilli were pathogenic just like the parent strain, and that both streptomycin and isoniazid were active against the infection with them.

Strains of Mycobacterium tuberculosis resistant to seromycin, streptovaricin, streptomycin and isoniazid were all susceptible to 1.6 mcg./ml. of kanamycin according to W. Steenken et al., whereas the neomycin- and viomycin-resistant strains were resistant to 1000 mcg./ml. of kanamycin. The drug had definite but limited bactericidal activity. The drug was much less active *in vivo* than isoniazid and slightly less than streptomycin. Kanamycin is far less toxic in the guinea pig than neomycin, even though it showed cross resistance with latter drug.

(*Continued on page 229*)

THE NEW COLLIERE FACTORY

BY FRANCIS CHILSON, INDUSTRIAL CONSULTANT

In Mexico City along the boulevard that leads to Xochimilco the new plant of Establecimientos Mexicanos Colliere S.A. was recently opened. This beautiful plant of a hundred thousand square feet of space is the third plant which the writer designed for the Colliere interests. The others are in Santiago, Chile, and Lima, Peru. All plants manufacture cosmetics and pharmaceuticals under their own brands and the company also acts as manufacturing and sales agent for some of the largest pharmaceutical and cosmetic firms in the U. S. as well as in Europe.

The Colliere family is French but they have been operating in Central and South America for fifty years. The present president of the firm, Bernard Colliere, is in his middle thirties; is a graduate of the Sorbonne and was a member of the French underground during World War II. Since Bernard took over as president following the death of his father a few years ago the company has been revitalized and sales have sky-rocketed.

This increase in business necessitated a new plant. The old plant was a multi-story building practically in the heart of Mexico City. It had no land for expansion and further, since it was built with an open court or patio so beloved by many architects in the center of the building, the problems of material handling, supervision and control were appalling.

A survey of plant sites was made in and around Mexico City and a site of nine and a half acres along the Calsada de Xochimilco was selected. It is an excellent site in an attractive area with plenty of water, power, sewerage and other site facilities. Having determined the size and type of building to be erected, preliminary but quite detailed specifications were drawn and six of the best known builders in Mexico invited to submit bids. These were carefully screened for credit rating, industrial experience, integrity and reputation with their former clients. A first-rate architect was employed but his responsibility was limited to interior and exterior decoration, landscape gardening, materials selection and construction supervision. The basic design and interior layout of the structure was under the supervision of the writer and the architect was told that he could make no alterations whatever without my approval. The architect, a Mr. Ituarte, proved to be an exceptionally able and cooperative man with the result that we formed a most amiable relationship and the finished plant is as much a credit to him as it is to me.

The building is a one-story structure with the general office area and the personnel facilities area forming an L around and two of the main facades of the principal structure. The office wing contains the executive offices, the general office, sales training rooms, office toilet areas, file rooms and other related facilities. The personnel area contains the medical department, personnel office, a union office which is required by Mexican law, an executive's dining room, cafeteria and kitchen, toilet and locker room facilities for factory men and women, maintenance shop, boiler room, a nursery for the babies of women workers—another element required by Mexican law—and an apartment for the plant guard who is in residence constantly. The office and personnel wings can be expanded independently without ever coming into collision with each other or with the main plant.

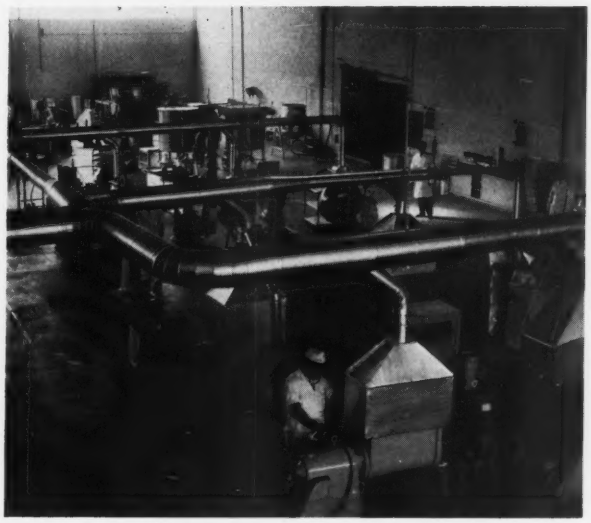
All personnel use a common entrance, officials as well as factory hands. On the left, forming a separate little island, is the personnel office and waiting room, the medical department and the guard's room. Factory personnel turn right down a circulation corridor in the personnel area, which runs straight through the building along the factory wall, to their locker rooms. Office personnel go straight ahead into a circulation corridor which leads to office locker rooms and into the general office. Officials enter their section though the marble and plate glass reception room into a short corridor off which their offices are located. Along this corridor interview rooms for visiting salesmen are established. Private offices are limited to officials and a secretarial bank is located immediately outside their offices. All other executives are located in a section of the open general office, which of course is sound-proofed.

The main factory and warehouse building is constructed of cinder block, brick and concrete. The interior is finished with tile 8 feet high. It utilizes a convolute roof of vermiculite concrete, and, to the best of my knowledge, this is the first pharmaceutical or cosmetic factory in the world to utilize such a roof. This roof has the virtue of permitting very wide interior spans, in this case 40 x 60 feet. Likewise, all interior trusses and struts are eliminated, so that the

(*Continued on page 230*)

Colliere factory, showing convolute roof, office and service wings.

The office wing and main entrance to the factory.



The tablet department of the Mexico City factory.

Colliere warehouse, which can be expanded easily.

The packaging department, showing the excellent lighting.

Finished stock room, which flows to packing department.

COURTESY AMERICAN CHOLESTEROL PRODUCTS INC.

SOLUBILIZATION BY MEANS

BY LESTER I. CONRAD, KALMEN MOTIUK, HENRY F. MASO

FROM THE RESEARCH LABORATORIES OF AMERICAN CHOLESTEROL PRODUCTS, INC., EDISON, NEW JERSEY

Solubilization is the name given to a phenomenon which brings into apparent solution materials that are otherwise insoluble in a given liquid medium. The presence of a colloid is prerequisite to this physical state, since it is the colloidal particles which incorporate the insoluble materials within or upon themselves. The original solid particle or liquid droplet to be solubilized, known as solubilizate, completely disappears as it is taken up, molecule by molecule, by the organized structure of the stable colloid itself (1). This structure, or micelle, is formed by all surface-active agents at and above a critical concentration, known as the Critical Micelle Concentration.

Since the present study is concerned with solubilization in aqueous media, all of the solubilizers included must be soluble in water and form colloids therein. The providing of the proper colloidal environment for the solubilization of a particular substance is the prime function of the solubilizer. In addition, the latter, which is always a surface-active agent, may have other effects which enhance its activity, such as cosolvency and specific complex formation. Although long recognized as a colloidal phenomenon, it is only recently that a physicochemical basis for solubilization was arrived at through the efforts of many investigators, notably McBain and his coworkers at Stanford University. Unfortunately, our knowledge of this field is still far from complete. Griffin (2) has shown that the hydrophile-lipophile (HLB) system of classifying surfactants is of some use in choosing solubilizers, although the relationships between HLB and certain solubilization factors are not in complete agreement.

In 1956 Moore and Bell (3) published some interesting generalizations which they feel hold true for a homologous series of solubilizers. Summarized briefly, these are as follows:

1—The amount solubilized increases directly with the polarity, cyclization and unsaturation of the solubilizate, and inversely with chain length.

2—The addition of inorganic salts to a solubilized system increases the amount of non-polar substances solubilized and decreases the amount of polar substances solubilized.

3—In a non-ionic series, the more lipophilic members favor maximum solubilization of low polar substances, and the more hydrophilic members favor solubilization of the substances which are more polar. In spite of many excellent studies on solubilization which have brought about an understanding of the mechanisms involved, at this date it is still necessary to carry out empirical research to arrive at practical answers in most cases involving solubilization.

The objective of this investigation was to evaluate several water-soluble, surface-active lanolin derivatives, for solubilizing such water-insoluble materials

as lanolin, constituents of lanolin and lanolin derivatives.

It was further desired to study the solubilizing effects of the surface-active lanolin derivatives on a variety of water-insoluble materials such as mineral oil, vitamin oils, perfume, hexachlorophene and other substances.

The problem has been approached from the formulator's viewpoint rather than that of the physical chemist in an effort to obtain formulation data of practical interest to the cosmetic and pharmaceutical compounder.

McBain's statement that "any material can be solubilized in any solvent by proper choice of solubilizing agent" (1) sounds broad and exaggerated when, as a novice, one starts working in this field. However, as he progresses he begins to realize the tremendous possibilities offered by the ever growing number of solubilizers.

The great value ofthe lanolin-derived solubilizers as opposed to the large mass of solubilizers available today, lies in the unusual combination effects which

OF LANOLIN DERIVATIVES*

these non-ionic lanolin products provide for formulation purposes. The emollient and conditioning properties usually associated only with oil-soluble materials are obtained from the solubilizer as well as from the solubilizate. These unique combinations provide a variety of aqueous systems ranging from crystal clear gels to thin solutions. Another interesting practical application is the incorporation of emollient lanolin products in both phases of emulsions; in the oil phase by solution and in the water phase by solubilization. Active ingredients such as vitamins, hormones, antiseptics and fungicides may be incorporated in the same manner in both phases to obtain fortified effects.

Generalizations

In conducting the present investigation of lanolin-derived solubilizers, the following generalizations which had resulted from laboratory studies of the past two years were applied:

1—The presence of certain functional groups in the solubilizer influences solubilization: namely, hydroxyl groups, ether linkages formed by the alkylene oxide chains, unsaturated bonds mainly due to the acid radical, and ester linkages. The hydrophilic and lipophilic properties which are important in solubilization, are determined by these groups as well as by other factors. The solubilizing power of a given substance is due to the balance of properties brought about by the functional groups, the molecular weight of the constituents, and the hydrophilic or lipophilic groups. It is therefore necessary to try homologs of a given compound regardless of the fact that the original compound appears to be a poor solubilizer.

2—It is often advisable to use a mixture of two or more solubilizers since the product may be solubilized more readily by the mixture. In difficult cases a co-solvent is helpful to obtain a clear solubilized preparation.

3—Once a compound or a mixture of compounds shows promise as a solubilizer, it is advisable to study the solubilizing effect over a range of ratios: solubilizer to solubilizate. These ratios are dependent on the amount of substance which one wishes to dissolve in a given solvent. A ratio which is sufficient to solubilize a substance in one concentration may not be adequate to solubilize the same substance in a different concentration. It is therefore necessary to know the final concentration desired and to aim at solubilization at this concentration.

4—While one may fail to prepare a clear dilute solubilized mixture directly, clarity may often be obtained by diluting a viscous concentrated solution stepwise to the desired level. This precaution is not always required, as some combinations of solubilizer and solubilizate do form clear solutions in water when prepared directly.

5—Mutual solubility of solubilizer and solubilizate is not a prerequisite for solubilization in water.

6—The mixture of water, solubilizate and solubilizer often has to be heated to form a solution; the optimum heating time and temperature varying in each case. Since many of the mixtures have a negative solubility, their solutions may be cloudy at high temperatures and clear at room temperature. This clarification being slow to develop, it is advisable to observe the appearance after twenty-four hours at room temperature. Slightly opalescent solutions may often be made crystal clear by the simple expedient of rapid cooling.

It is obvious from the above that the conditions under which a material is solubilized have a marked influence on the appearance of the finished product.

Materials

Preliminary studies yielded interesting data with a wide variety of ethers and ester-ether lanolin-derived solubilizers. This led to the selection of the materials employed in the solubilization studies reported in this paper (Table I, p. 232). The code numbers in the left-hand column are used throughout this paper to identify the solubilizers described in the table. Ethy-

(*Continued on page 232*)

*Reprinted from the Proceedings of the Scientific Section of The Toilet Goods Association, Inc., No. 29, June 1958.

ROUGES

BY MORTON H. DANIELS
TECHNICAL DIRECTOR, PARIS COSMETICS, INC.

By applying tinted earths and the stains from bark, roots and berries to her hair, eyes, cheeks and mouth, woman has always endeavored to make herself outstanding and attractive to the opposite sex. Although the efforts of the ancient glamor girls could be termed "grotesque" by comparison to modern standards of good grooming, history reveals their complete success in amorous conquests. The blush look, the flush look, and the pale look have all accounted for the rise and fall of popularity of rouge during the last half century. Cream and liquid rouge have gained favor over the compressed tablet in the last few years.

A product is no better than its components! Purchase only the best grades available from reputable sources of supply, and comply strictly to the regulations of the F. D. A., particularly sections: 303c, 601e, & 602 a, b, c.

In compounding a dry rouge the operator must strive for the desirable features necessary for good end results.

(a) Clear color—without the tendency to become muddy or drab.

(b) Complete coverage—avoid excessive opacity. Strive for the "natural look".

(c) Good pay-off—without excessive residual dust.

(d) Firmness—the tablet to be sufficiently firm to withstand impact without developing cracks, but not to develop "hard spots" that shine when rubbed with puff.

(e) Perfume—select fragrance with care to avoid irritation, and present color change particularly with aniline lakes.

A typical starting formula might be:

WHITE BASE	
Talc	52.0
Titanium dioxide	7.5
Micro kaolin	15.0
Zinc oxide	3.5
Barium Sulfate	18.0
Zinc stearate	4.0

Depending on the shade to be created or matched, from 3 to 15 per cent of earth and/or aniline lakes, and from 85 to 97 per cent of white base are mixed together in a ribbon blender equipped with a rotary brush sifter and turned over several times. . Mix for one-half hour and pass once through a pulverizer equipped with a 0.013 herring bone slot screen. Transfer the first grind to a change can pony mixer and spray or "drip" in the binder.

The binder may be one of several types:

(a) Water soluble gums or mucilage—e.g. 1 or 2 per cent preserved solutions of acacia, tragacanth, karaya, quince, guar, carragheen, alginates, CMC or PVP. Binders of this type should be tested with each color separately to establish the degree of "color bleed" or fading.

(b) Moisture Repellent Types include: Light mineral oil petrolatum, isopropyl palmitate and/or myristate, lanolin, lanolin esters, butyl stearate used alone or in conjunction with one or more of the same type. A small percentage of water and wetting agent may be added.

(c) Emulsion Binders—usually include water, preservative, humectants (propylene glycol or sorbitol) mineral or vegetable oils, and emulsifiers such as glyceryl or propylene glycol monostearate and perhaps a metallic soap. Although this type has the advantage of uniform oil and water distribution, it dries more slowly in the finished tablet.

(d) Dry Binder—one or more of dry metallic stearates. Although tablets pressed with this binder result in better adhesion and fairly good texture, the risk of personal hypersensitivity is increased due to the alkalinity of some metallic stearates.

The writer prefers type (b) binder and a suggested starting formula might be:

65-75 vis. Mineral oil	30.0
Tween 20 or 60 (3)	20.0
Sodium benzoate	0.2
Water	q.s. to 100.0

Heat a small portion of the water, add the sodium benzoate, dissolve, add the balance of cold water. Store preservative solution separately. Mix mineral oil, Tween and perfume 0.25 per cent together and add preservative solution just prior to wetting the powder. From 25 to 50 cc. of binder is used with the powder previously described. A complete formula may be presented as:

White Base	85-97%
Pigment and/or Lakes	3-15%
Perfumed Binder	25-50 cc per lb. of dry material

The amount of binder used depends upon the equipment selected for pressing and the method of drying chosen. Transfer the wet and sifted rouge mass to a pulverizer equipped with a 0.026 herring bone slot screen and pass through twice. Store the mass in double polyethylene bags (to prevent evaporation of binder) till ready for pressing.

Prepare the compact discs by spraying lightly with a dilute solution of water soluble adhesive and dry thoroughly. For manual or foot presses, first remove excess air by pressing wetted rouge between several layers of rough tissue paper. Next pre-mold tablets by lightly tamping a fixed volume of powder into each tin. Finally place the disc in the female die equipped with a pressure pad of para gum or medium textured foam rubber. Slow uniform pressure is applied to the surface of the tablet by the male die, which should be entirely free of scratches or dents, and equipped with latex or thin rubber diaphragm stretched taut. Fast or hard descent of the male die will result in tablets having hard centers and porous edges, which when dry, develop cracks easily, and may develop hard shiny spots with poor pay-off. For large volume runs, automatic tableting presses should be used. Two precautions are essential. The male die should be highly polished and equipped with a device to remove the excess powder after each cycle.

Pressed tablets should be stored in shallow trays and placed upon racks with sufficient room between the tiers to insure uniform drying. Dry slowly in constant temperature to avoid crusting and blanching, particularly of light shades. Do not dry in sunlight or in the presence of extreme heat.

Cream Rouge

Preference for cream rouge is based on better spreading without showing lines of demarcation. This is particularly true with rouges with a creamy foundation.

Typical suggestions for anhydrous, emulsion, and vanishing types might be:

	ANHYDROUS	VANISHING		EMULSION
White petrolatum	55.00	—	—	23.00
Stearic acid	—	2.00	17.50	—
Beeswax	2.00	—	—	11.80
Cetyl alcohol	2.00	2.00	2.50	5.20
Wecobee SS (1)	7.00	—	—	—
Super Hartolan (2)	0.50	0.50	1.00	0.70
Carnauba wax	5.65	—	—	0.80
Tween 20 or 60 (3)	—	2.00	—	—
Isopropyl myristate	8.00	—	1.00	2.00
Crystal O castor oil (4)	8.00	—	—	—
Mineral oil 65-75 vis.	—	—	—	20.00
Glyceryl monostearate	—	10.00	—	—
Methyl p-hydroxybenzoates	0.10	0.20	0 20	0.25
Glycerin	—	4.00	5.00	—
Propylene glycol	—	3.00	—	—
Sorbitol	—	—	5.00	—
Potassium hydroxide	—	0.20	0.90	—
Borax	—	—	—	0.75
Oleic acid	—	—	2.00	—
Water	—	68.10	57.40	28.00
Pigments	7.50	7.50	7.50	7.50
Bromo acid-D & C red 21 or D & C orange 5	0.25	0.50	—	—
Albatex (5)	4.00	—	—	—
Perfume	q.s.	q.s.	q.s.	q.s.

(Continued on page 248)

Regulation of Biologicals

BY PARKE M. BANTA
GENERAL COUNSEL, DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

The basic Federal law according to which Federal regulation of biologicals is accomplished, through licensing, seems to have been referred to as "The virus law." It is now a part of the Public Health Service Act, as amended, and commonly referred to as the biologic control provisions of that Act.

Under the statute the manufacturer of any virus, serum, toxin, antitoxin, or analogous product applicable to the diseases or injuries of man and shipped for interstate sale, export or import, is made subject to Federal Licensure to protect the public health.

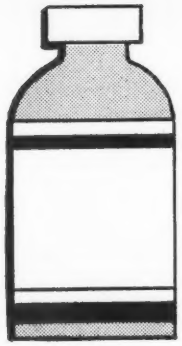
The statute originated in 1902 at a time when biological drugs were coming into widespread use in this country. It appears that products of this type were subject to control or regulation by law at least in France, Germany, Italy and Russia, as early as 1895. I found nothing to indicate whether or not, in the passage of the original "virus law", we were motivated to any extent by what other countries were doing in this field.

The result was a statute which applied to "any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention and cure of diseases of man." In 1944 there was added arsphenamine or its derivatives or any other trivalent organic arsenic compound. Thus in its present form, the statute prohibits any person from sending, carrying or bringing any such drug for "sale, barter, or exchange" from one State to another, or to export or import it, or from selling it in the District of Columbia, unless first, it is produced at an establishment licensed for the production of the product by the Secretary of Health, Education, and Welfare and unless, also, the package bears a label giving the proper name of the product, the name, address and license number of the manufacturer and the date beyond which the drug cannot be expected to yield its specific results. In addition, the statute prohibits falsification of the label of any package of a product, and interference with Public Health Service employees carrying out their duties under the Act, including the inspection of establishments engaged in the preparation of the products. Persons who violate any of the provisions of the Act are subject, upon conviction, to punishment by fine not exceeding $500 or imprisonment not exceeding one year, or by both such fine and imprisonment.

You will note that unlike certain provisions of the Federal Food, Drug, and Cosmetic Act, this statute is not violated simply by shipping for sale impure or adulterated products. Such action is prohibited by the Federal Food, Drug, and Cosmetic Act. The violation under the Public Health Service Act is the shipment for sale of *unlicensed* products or those not labeled as required by the statute. On the other hand, it is no defense that an unlicensed product shipped for sale is in fact safe, pure, and potent or that it is shipped for a limited use such as research, unless of course, it is being distributed interstate without sale, barter or exchange, such as the material for the poliomyelitis vaccine field trials in 1954.

The protection of the public and the essence of the statute therefore lies in the basis on which licenses are issued and can be suspended or revoked. Such issuance, suspension, or revocation is controlled under the statute by regulatory "standards designed to insure the continued safety, purity, and potency" of the product. These terms were added to the statute in 1944 in order to provide a specific legislative guide for the exercise of the regulatory authority. The regulatory standards must be adopted by the Surgeons General of the Army, Navy, and Public Health Service and approved by the Secretary of Health, Education, and Welfare. The inclusion of the three Surgeons General was, apparently, due to the feeling in 1902 that a group judgment was desirable and possibly because of the considerable military experience

*Before Section on Food, Drug and Cosmetic Law, New York State Bar Association, January 29, 1958.



in the use of this type of drug. There is today, of course, some question of the need for continued participation by the military services in view of the considerable development of Public Health Service research experience and capacity and the Service's broad responsibilities for the Nation's health from the Federal point of view. The military services have proposed to Congress that the Act be amended so that participation by the Surgeons General of the Army and Navy will not be required.

The regulations establishing the controlling standards are adopted, of course, in accordance with the requirements of the Administrative Procedure Act and thus with opportunity to the public to participate through notice of proposals published in the Federal Register. The regulations both as to standards to assure safety, purity and potency and also as to procedures for the issuance, suspension or revocation of licenses are contained in Part 73 of Title 42 of the Code of Federal Regulations. The regulations dealing with the standards are essentially of two types: First, those applicable to all products covered by the Act and second, additional standards for specific products. The additional standards to date apply to trivalent organic arsenicals, poliomyelitis vaccine and adenovirus vaccine, and there is in process for final adoption additional standards for Whole Blood (Human). Other additional standards will be proposed from time to time for particular products whenever in the scientific judgment of the responsible Public Health Service personnel the general regulations are not adequate to insure the continued safety, purity and potency of the product involved.

On the recommendation of the Director of the National Institutes of Health, responsibility for the administration of the statute has been placed by the Surgeon General of the Public Health Service, with the approval of the Secretary of the Department, in the Division of Biologics Standards of the National Institutes of Health at Bethesda, Maryland. While the formal issuance, suspension or revocation of a license is the responsibility of the Secretary of the Department, the day-to-day administration of the statute is now, as it has always been, fully in the hands of professional medical personnel and in a research context.

This fact is perhaps the key to what to lawyers must appear to be a rather remarkable record: Although the statute establishes a Federal licensing program, one of the more comprehensive types of Federal control, as far as I can determine there has not been since the enactment of the statute in 1902, any litigation directly involving its application or interpretation; no one has been penalized for its violation nor so far as I know charged under its penalty provisions with any violation of any of its provisions. Moreover, I am informed that no license has been suspended or revoked over the protest of the licensee. The law has been administered by scientists dealing with their counterpart scientists in the industry concerned and primarily by the medical-scientific discipline common to both.

I think it fairly obvious that the overriding factor in this relationship is the special nature of the product and the type of purchaser. In general, the products are used solely by the medical profession and involve serious and immediate risks to the patient unless extraordinary care is used in their preparation. It is not a field for less than the expert. Perhaps nowhere in Government is the objective of the manufacturer and of the regulating agency so near the same.

The value of this type of relationship to public health is perhaps best evidenced by the fact that often the licensee is the first to inform the Public Health Service of an accident or of information which raises some question as to a product's safety. The licensees generally seek to obtain the assistance of the Service in taking every precautionary action, and if it becomes necessary, remedial and corrective action, and obviously such relationships make possible the prompt and effective action which seems always to have been the rule.

A further illustration of the value of the cooperative relationships existing between the administrators of the law and the licensees is provided by the Asian influenza outbreak in 1957. While the work of the Army in isolating and identifying the new strain of influenza placed this country in a position, for the first time in history, to prepare in advance for an influenza epidemic, there remained the considerable task of developing promptly an effective vaccine in large quantities. Here the Public Health Service provided the seed material and worked on the scientific problems involved with those manufacturers that had previously been licensed to produce influenza vaccine involving other strains. A protective product was thus made available to the public in a much shorter time than would otherwise have been possible—a unique accomplishment in preparation for an influenza epidemic.

There are, of course, problems. We have, for example, been working with the Surgeon General and the Director of the Division of Biologics Standards

(*Continued on page 239*)

HARD TO GET
African Rarities

BY STEFFEN ARCTANDER. COLGATE-PALMOLIVE CO.

Vanilla vines on Pandanus, Reunion.

Yes, you are quite right. Almost any raw material can be "hard to get". So let us confine this report to a few of those materials, which are always scarce, little known, and yet of perfumery interest because of their particular effect.

Hundreds of essential oils and absolutes are produced in annual quantities of less than 100 lbs. Why? For various reasons. Some of these products are prepared specially for one or a few customers, who use them in their current specialties, and who probably want to keep these materials for themselves. Materials with "intriguing and inimitable" effects, as we so often read, when a rare perfume oil is described. Other oils are produced experimentally, some cannot be produced in larger quantities because of inavailability of the natural raw materials in question. Some oils or absolutes come in so small yields that even fair amounts of natural raw materials seem to vanish when the oil or the absolute is prepared. Price and labor availability are other important factors in the production of rare oils in small quantities.

In Europe, particularly in France, a very large number of absolutes are produced from flowers and other plant materials not exploited elsewhere in the world. These are all "hard to get", unless they deal with new, experimental perfume oils, which the supplier tries to promote among his customers.

But in the tropical countries, we find a wealth of rare flowers and plants, many of which have not yet been exploited for their perfumes. Below, I shall mention a few which have all been known for many decades, and still remain "hard to get", but actually are available.

In this country oils such as cassia and star anise have become "hard to get" for quite other reasons, but fortunately, the shortage of these oils has not affected the perfumery market to any noticeable degree. Or, as some perfumers will put it: "Cassia oil was already so adulterated that it had lost interest with us". And the production of pure, synthetic, N.F. Anethole has now reached a maximum of effectiveness as far as olfactive and organoleptic purity is concerned.

During various trips through Africa and the Middle East I had the opportunity of meeting some of

Plumeria Alba, the white Frangipanni, the fragrant flowers of which can be smelled hundreds of feet away. A model for early perfume types. (Uganda). Common all over the tropics.

Michelia Champaca, the true Champaca, Nossi-Be.

A flower of Terminalia Cheluba, N. O. Combretaceae, producing Myrobalans, and a bark with high tannin-content. The flowers are extremely fragrant, but not used in perfumery. (Madagascar).

these "rare" perfume plants. In the perfumery review "Les Parfums de France" 1937-38, Monsieur L. Joly, internationally known botanist and scientist, published a list of perfume plants from tropical Africa. He mentioned over 300 plants, most of which were so far unknown, and are still today hardly investigated thoroughly. That tells us that we can still expect many pleasant surprises from Mother Nature simultaneously with the increasing number of synthetic perfumery materials now available.

According to Gildemeister & Hoffmann's "Die aetherischen Oele", a total of 1,371 essential oils were "known" in 1931, i.e. these oils had been produced, investigated, and reports published. At the end of preparation for the publishing of the new edition (1957-——) of this comprehensive work, a further 1,000 essential oils are known, they state. Which brings us to a total of 2,371 known essential oils of today. The actual number is probably still higher, if we consider the oils investigated in agricultural research laboratories all over the world. Only a fraction of these experiments and results are known to the perfumers. Unfortunately, a really objective, purely scientific and reliable collection of such—and other—publications from all over the world does not exist—although in this aspect unsurpassed, old "Schimmel's Berichte", now called "Miltitzer Berichte" is available to a narrow circle of perfumers or perfume laboratories.

By far the majority of the 2,371 essential oils are "hard to get", and therefore I will confine myself to mention a few of those which I have met during various motor trips through Africa and the Middle East:

Popowia cape oil has been known for at least 50 years, and is still used by a few French perfume houses. It was originally distilled from the leaves of a climbing vine, found wild-growing in West Africa around Senegal and south to the Ivory Coast. Just as some enterprising and farsighted pharmaceutical companies recently sent out "talent-scouts" to the tropics to interview medicine-men, to trace old tales of wonder drugs at native villages—and actually have found very important, and effective drugs for the benefit of millions of hopelessly sick people—just similarly were young French botanists sent on excursions throughout the colonies many decades ago (and they are still scouting!) to trace perfume plants often well known by the natives since antiquity.

I first met the popowia cape on a very early trip, and I lacked sufficient advance information. I thought that the flowers were exploited for perfume because of their fragrance. But as said it was the leaves. The tropical West Africa is very rich in plants of this family—anonaceae—to which also ylang-ylang belongs. It might be of interest to see whether the french perfume oil producers in the Fouta-Djalon district will be interested in these plants which all have

(*Continued on page 240*)

Stephanotis Floribunda, a native of Madagascar, is a vine from the dense bush, whose flowers exhale a sweet, tuberose-honeysuckle-like fragrance. Also called "climbing tuberose."

Nymphaea Alba, a white water lily. Its beautiful flowers have a most delicate perfume, but are not exploited. This is a danish variety of the Water Lily.

THE STUDY OF HUMAN HORNY LAYERS*

BY PETER FLESCH, M.D., Ph.D., ASSOCIATE PROFESSOR OF RESEARCH, DERMATOLOGY
SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

Figure 1—Experimental set-up to measure the flow-rate through a column of pulverized scales. (See text.)

A year ago a question was raised about the plasticizing effect of water for dried keratin (1). The answer, by a noted cosmetic chemist, referred to Blank's work (2) and read in part: ". . . Water is the best softening or plasticizing agent for hair and epidermis . . . The water imbibition of keratin is . . . closely proscribed by the disulphide linkages." While this statement was correct, it was only half-true. By listing hair and epidermis in the same category, the writer missed an essential point. Hair consists almost entirely of keratin, the insoluble protein, while the epidermal horny layer (we assume that this was being discussed, since reference was made to Blank's work) has a keratin content of only about 60 to 70 per cent. The remainder consists of water-soluble compounds. A large part of the hygroscopocity of the horny layer resides in this water-soluble fraction. The water-holding ability of the *stratum corneum* is not primarily dependent on its disulfide linkages which are far less numerous than in hair, but is controlled by the non-keratinous soluble components whose water-binding capacity has been the subject of Blank's work.

This sort of error is quite common. It permeates dermatologic nomenclature and thinking. In a recent review, Shelley and Arthur (3), in discussing the "keratinoctye" (a term for the epidermal cell), write that "the physiology of the keratinoctye is basically the story of the holocrine secretion of a fibrous protein." Both the statement and its attribution to me, are erroneous.

Another striking proof of the confusion in this area is the indiscriminate use of the word "keratolysis." This term literally means dissolution of keratin; a keratolytic agent therefore should denote a compound which partially or completely solubilizes keratin, such as alkalis or thioglycolate. However, the word keratolysis is seldom used in this context. In dermatology, a keratolytic agent is a compound which breaks up the horny layer. Dispersion of the horny layer, however, does not necessarily entail an attack on the keratin molecule; it may well result from a dissolution of a "cementing" substance between the cornified cells. The study of this hypothetical cementing substance, of its nature and functions is one of the most important pending tasks of investigative dermatology.

The present paper deals with methods used by us to measure the dispersal of the horny layer and with some studies of the cementing matrix between the horny cells.

Experimental

I—MEASUREMENTS OF FLOW RATES ACROSS PULVERIZED HORNY LAYERS.

This method, briefly described in a previous publication (4), is based on measuring the time required for any oily liquid to pass through a column of pulverized horny material.

One hundred milligram samples of defatted, pulverized horny scales are packed into tuberculin syringes to the same height. Into the syringes, over the column of powdered horny substance, 1 ml. of an oily

*Reprinted from the Proceedings of the Scientific Section of The Toilet Goods Association, Inc., No. 29, June 1958.

liquid is poured. Then we measure the time required for the fluid to pass through the powdered scales (Figure 1). For the sake of simplicity, we will refer to this time as "flow rate." Although at first sight the method appears to be crude, fairly uniform results may be obtained with it, as indicated in Table I. The

TABLE I

Flow rates, expressed in minutes, of squalene through scales from a patient with neurodermatitis.

	Water	Extracting medium 10% urea	0.2% allantoin	0.2% aluminum chlorhydroxy allantoinate
Exp. #1	20	23.5	9.5	19.5
Exp. #2	19	20	10	19.5
Exp. #3	19	22.5	11	18.5
Exp. #4	24.5	—	—	—

secret of getting consistent data lies in preparing the specimens and measuring the flow rates under strictly comparable and rigid conditions (pulverization to standard size in Wiley-mill, defatting under similar conditions with ether, scrupulously clean syringes, uniform distribution of powder, etc.).

With this method a number of variables may be measured. These are as follows:

A—Flow rates of various oily substances

Among the fluids tested a definite order could be established, regardless of the type of horny scale used (normal or pathologic). The order from the fastest to the slowest flow rates is generally as follows:

1—Isopropyl myristate. 4—Oleyl alcohol.
2—Squalene. 5—Corn oil.
3—Perhydrosqualene. 6—Heavy liquid petrolatum.
7—Eutanol G. 8—Cottonseed oil.

A typical example of flow rates of various liquids is illustrated in Tables II and IV. No attempt has been made to restrict our studies to oils of similar viscosity, as this would have limited our work to relatively few substances. The fact that viscosity is only one of many factors influencing flow rates is readily visible from the list of substances in Table II.

TABLE II

Flow rates, expressed in minutes, of various oily liquids through pulverized scales of patients with keratoderma plantare, exfoliative dermatitis and psoriasis.

Substance tested	Type of scale Keratoderma plantare	Exfoliative dermatitis	Psoriasis
Isopropyl myristate	0.5	18	5
Squalene	0.75	72	12.5
Perhydrosqualene	2.5	58	38
Oleyl alcohol	3	90	25
Corn oil	5	106	49
Heavy liquid petrolatum	9.5	—	—
Cottonseed oil	10	120	52

TABLE III

Flow rates, expressed in minutes, of different oily liquids through various types of pulverized horny layers.

Substance tested	Type of horny layer Callus	Psoriasis	Ichthyosiform erythroderm
Isopropyl myristate	0.1	5.5	33
Squalene	1	58	100
Perhydrosqualene	2.5	16	120
Corn oil	3	56	137

B—Variations in flow rates among different specimens

The most remarkable finding in these experiments

Figure 2—Scale from a patient with ichthyosiform erythroderma, after extraction with 1. water, 2.10% urea, 3. 0.2% allantoin and 4. 0.2% aluminum chlorhydroxy allantoinate. Magnification x 45.

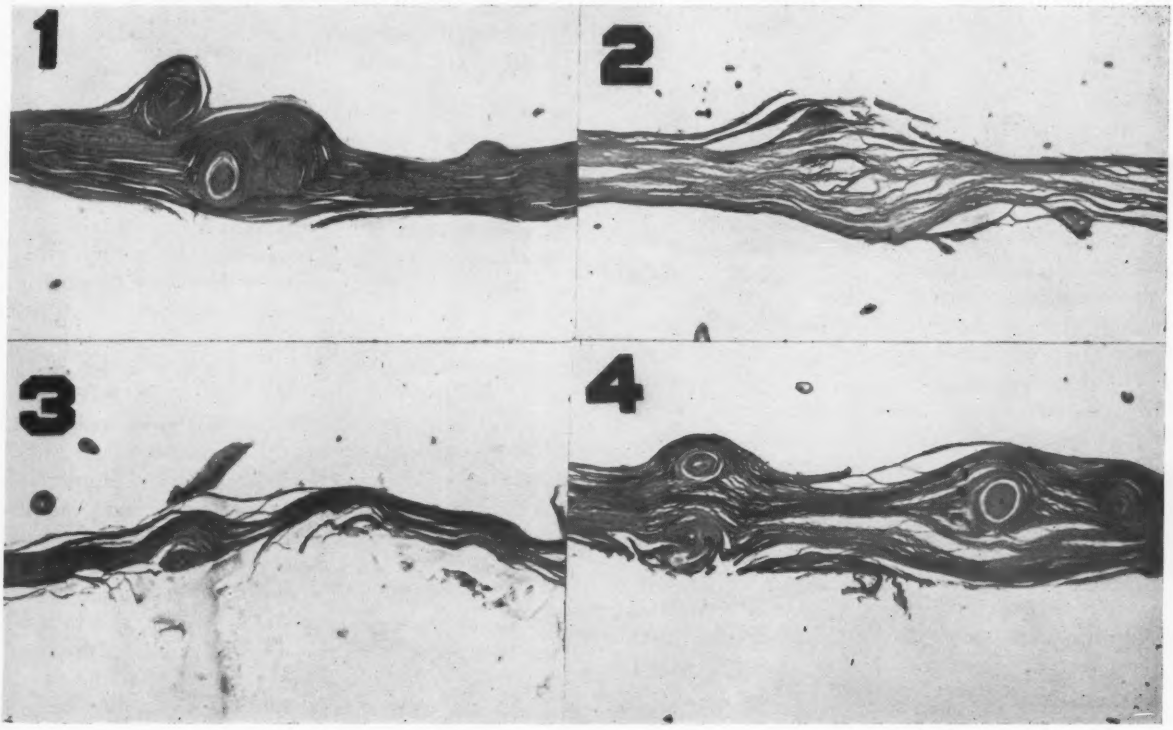


TABLE IV

Flow rates, expressed in minutes, of different oily liquids through pulverized scales of a patient with keratoderma plantare after extraction of the scales with various agents.

Liquid tested	Extracting medium			
	None	Water	75% lithium bromide	10% Duponol
Squalene	16.5	10.5	10	5
Perhydrosqualene	52	23.5	10.5	67
Isopropyl myristate	10.5	3	0.75	5.5
Oleyl alcohol	84	21	16.5	29
Corn Oil	51	42	13	37
Cottonseed oil	62	34	21.5	55

was the constant and striking difference between normal and pathologic specimens, regardless of the type of oil tested. For normal specimens we used pulverized callus. Although callus is not necessarily representative of normal horny layers, the amounts of pulverized scales required for performing these studies precludes the use of horny layers scraped from non-callused skin areas. It is not always realized that the collection of surface scrapings without admixture of lanugo hairs is a very difficult task.

The pathologic specimens included scales from patients with psoriasis, ichthyosiform erythroderma, exfoliative dermatitis of unknown origin, neurodermatitis and keratoderma plantare. Without exception, the flow rates through pathologic specimens were tremendously retarded. It seems that the most coherent and confluent scales give rise to the most protracted rates of flow. Thus in a case of ichthyosiform erythoderma with large armor-like horny plates, the flow rates were 40 to 100 times as long as in callus. A severe case of exfoliative dermatitis also yielded slow rates of flow, while in psoriasis a greater fluctuation of values was observed, all of them above normal. (Tables II and III).

C—Effect of different dispersing agents.

To test the effectiveness of various agents which disperse the horny layer, the defatted and pulverized scales were incubated for 24 hours in the following media: Water, 10 per cent urea, 10 per cent Duponol®, 75 per cent lithium bromide, 0.2 per cent allantoin and 0.2 per cent aluminum hydroxyallantoinate* solutions. At the end of the incubation period, the scales were washed 3 times with water, 3 times with absolute alcohol, 3 times with ether and dried at 37°C. The pulverized and defatted material was packed into syringes in the usual manner and the flow rates determined. In one set of experiments the defatted scales were first extracted, then dried and pulverized. This more realistic reversed procedure gave the same results as the usual method of extracting the scales in their pulverized form.

The following general conclusions were reached:

1—After incubation with any of the extracting agents, including water, the flow rates became greatly accelerated. The only exception was Duponol; after treatment with this detergent, the flow rates usually became prolonged.

2—Of all the dispersing agents tested, lithium bromide reduced the flow rates most markedly. (Tables IV and V).

TABLE V

Flow rates of various oily liquids, expressed in minutes, through psoriatic scales.

Substance tested	Extracting medium				
	None	Water	75% LiBr	10% urea	0.2% allantoin
Isopropyl myristate	5	2	0.25	1.25	1
Squalene	12.5	4.5	1	3	3
Perhydrosqualene	38	18.5	2.25	27	6
Cottonseed oil	52	22	3.5	41	11.5
Oleyl alcohol	25	17.5	2.5	11	8
Corn oil	49	44	5	30	9.75

3—In this test allantoin compared favorably with a 10 per cent urea solution as a dispersant of the horny layer (Table V). Results obtained with aluminum chlorhydroxy allantoinate were not as uniform and this compound showed no superiority over allantoin (Table I).

4—The effect of the various dispersants varied with the scales tested. In some scales from psoriatics allantoin was ineffective. A typical example of the effects of extracting agents on flow rates in scales of psoriasis is shown in Table V.

II—MICROSCOPIC OBSERVATIONS.

Defatted scales were cut into 4 pieces and immersed into the following media for 24 hours: Water, 10 per cent urea, 0.2 per cent allantoin and 0.2 per cent aluminum chlorhydroxy allantoinate. After formalin fixation, the scales were sectioned and stained with hematoxylin eosin.

A typical sequence of microscopic changes is reproduced in Figure 2.

III—CHEMICAL STUDIES.

An index of the ability of various agents to break up horny layers is their capacity to extract free sulfhydryl compounds from scales. In previous studies we have shown that many pathologic scales contain high amounts of sulfhydryl (5) and that this sulfhydryl is attached to a soluble protein in the horny layer. The ability to leech out sulfhydryl compounds from the horny layer is a measure of the protein-dispersing capacity of the agent tested.

For this study, 5 to 10 mg. samples of pulverized defatted callus and psoriatic scales were incubated with the following agents: Water, 10 per cent urea, 0.2 per cent allantoin and 0.2 per cent aluminum chlorhydroxy allantoinate. Sulfhydryl was determined with Bennett's reagent (6). The results are shown in Table VI.

On the other hand, the release of free amino nitrogen into the extracting media cannot be used to estimate the capacity of various compounds to disperse horny layers. Already water will extract the max-

(*Continued on page 245*)

*Allantoin and aluminum chlorhydroxy allantoinate were obtained through courtesy of Schuylkill Chemical Company.

Packaging and Selling

One of the Individual New Package Designs

introduced by Cutter Laboratories for certain hospital and over-the-counter items. Although these individual designs differ from the standard design scheme of the regular Cutter line of packages, the styling is related to it by a subtle family resemblance.

...glamour in glass!

A world of beauty is a man's right, too

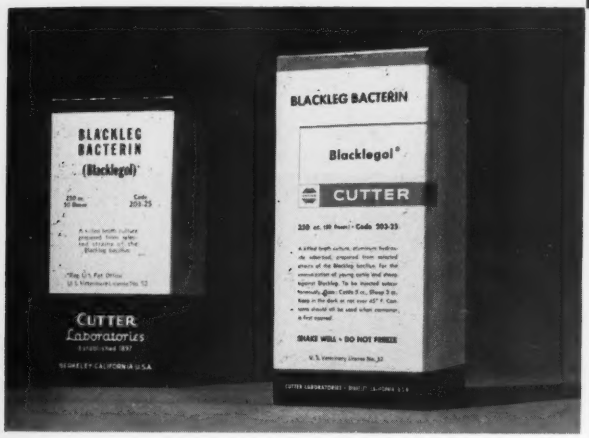
The tremendous market for masculine lotions, toiletries, and drugs makes male-styled containers a must. In gleaming, snowy opal, or crystal flint H-A *Private Mold* Containers are imagination in glass—and practical, too. At domestic prices, they add the glamorous prestige of more expensive imports to your men's products. And permanent "Deco-fired" labels can be economically applied at the time of manufacture. *Give your products a very special appeal*—call or write H-A, right now.

HAZEL-ATLAS GLASS division of CONTINENTAL CAN COMPANY

WHEELING, WEST VIRGINIA

THE WELL-CONCEIVED ETHICAL PACKAGE

In their quest for the ever more dramatic package, manufacturers of biologicals and pharmaceuticals must always guard against sacrificing the image of authority and reliability, which is the ethical firm's most valuable asset in marketing its products successfully. This is especially important in the case of prescription items, since physicians and pharmacists will naturally tend to favor the brands that most impress them from a professional point of view. Over-the-counter products, on the other hand, aimed as they



are at the ultimate consumer, provide different objectives, but here too design must be skillfully employed to win and keep consumer confidence.

One major producer of ethical and over-the-counter biologicals and pharmaceuticals that has demonstrated its alertness to this packaging problem is Cutter Laboratories, which maintains headquarters in Berkeley, California, and plants both in Berkeley and in Chattanooga, Tennessee. After several years of study and development, Cutter is currently completing a comprehensive package redesigning program of its ethical products to revitalize packaging features established for more than a half century.

The Cutter program will eventually include more than five hundred cartons, tubes and bottles varying widely in size and proportion. Its success is attributed largely to long and close cooperation between executives of the company and Walter Landor & Associates, San Francisco industrial designers who were selected for the task by Dr. Robert K. Cutter, president of the firm. Russ Moore, Cutter's coordinator of new product development, has had the responsibility of maintaining effective liaison between the company and the design organization.

Since its founding in 1897, Cutter Laboratories has evolved serviceable packaging. The principal identifying features, such as the Cutter shield and the white, blue and black color format, are familiar to physicians, veterinarians and pharmacists throughout the world.

Surveys among pharmacists and close analysis by the Landor design group, however, revealed serious deficiencies in the packages conceived as merchandising tools. For one thing, it was found that the enormous potential of the Cutter trademark was far from being completely realized: the shield appeared in different places on various packages, and on some packages it did not appear at all. Equally important, no attempt had been made to relate the trademark to registered trade names used by Cutter for many of its products. It was also felt that such vital packaging components as information regarding quantities and proper use needed skillful redesigning.

In sum, both Cutter and the designers agreed that the packages required greater integration, both individually and as members of a large family line, and at the same time called for an up-to-date, scientific appearance that would reflect the company's high standing in the ethical field. Consequently, it was considered essential that the new packages achieve these objectives within a framework of over-all resemblance to the old.

In a sense, the first steps taken by the designers

To package your product with personality, choose a versatile Du Pont ALATHON®

POLYETHYLENE RESIN

TRANSLUCENT

Roll-on container molded of ALATHON for Revlon's "Hi and Dri" deodorant is translucent, with a lacy design surprinted in white. Containers of ALATHON are lightweight and unbreakable. They are also inert to most chemicals and resistant to stress-cracking. ("Hi and Dri" container molded for Revlon, Inc., New York, by Wheaton Plastics Company, Mays Landing, N. J.)

OPAQUE

Roll-on container molded of ALATHON for The Wm. S. Merrell Co.'s "Rolief", poison-ivy and insect-bite lotion, is opaque white with a screw-on cap. The impermeability of ALATHON keeps products fresh and effective. Moreover, ALATHON is tasteless, odorless and non-toxic, and seldom becomes brittle or deteriorates. ("Rolief" container molded for The Wm. S. Merrell Co., Cincinnati, by Wheaton Plastics Co.)

There are a variety of different ALATHON polyethylene resins, each tailored for a specific need. Consult with your supplier about selecting the ALATHON that best meets your requirements. Or write to: E. I. du Pont de Nemours & Co. (Inc.), Polychemicals Department, Room 118, Wilmington 98, Delaware. In Canada: Du Pont Company of Canada (1956) Limited, P.O. Box 660, Montreal, Quebec.

POLYCHEMICALS DEPARTMENT

DU PONT

REG. U. S. PAT. OFF.

BETTER THINGS FOR BETTER LIVING . . . THROUGH CHEMISTRY

epitomize the entire restyling program. By subtly altering the Cutter shield and joining it to a larger version of the company logotype, a greatly strengthened trademark was provided for the brand.

The color combination was similarly modified. By narrowing the black band at the bottom of the package, the designers increased the white area. This, combined with the change-over to a lighter, "surgical" blue, considerably enhances the medical look of the containers.

A major objective of the redesigning was to relate the Cutter signature closely to the trade names or, in cases where no trade name is used, to the technical names of products. It was also felt desirable to allow due emphasis to Cutter trade names themselves. In the case of biologicals, the National Institutes of Health prohibit larger or bolder type faces for trade names than those used for technical names.

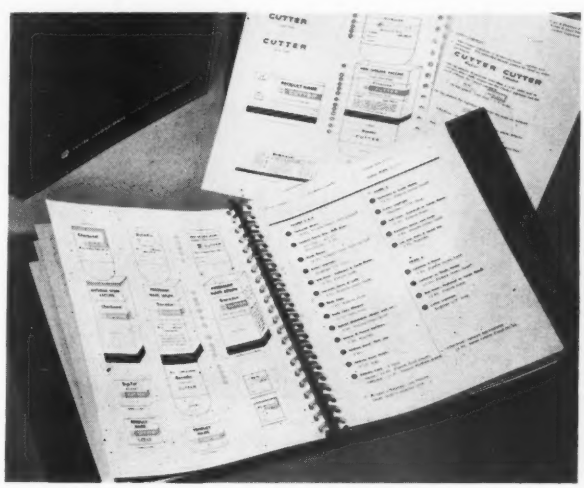
The Landor organization developed a skillful treatment for the principal identification area which achieves these objectives within this strict limitation. A frame formed by precise blue lines encloses the trade name and the Cutter signature, immediately adjacent to each other, while the technical name appears outside and above the frame. For products having no trade names, technical names occupy the frame. In either situation, the product title and the company trademark are joined in the mind's eye of the beholder.

The designers have extended the box treatment over on a side panel for added dimensional effect. On most of the packages secondary information, formerly found on all Cutter package surfaces, has been organized on front and back panels only (on the company's veterinary packages the back panel is usually reserved for Spanish-language identification). This step leaves the side panels wholly white and free of copy, another device in imparting a clean, scientific appearance to the package.

The pharmacist's convenience was taken into consideration in the design of top panels, since these are the principal identification areas for refrigerated items, such as most biologicals. A modified version of the front panel box treatment is employed, with color coding to designate Alhydrox, standard and alum precipitate products. As on the front panel, dosage and code numbers are set close to the main identifying area.

A unique feature of the program is the Cutter Package Design Manual, which the Landor organization developed as a permanent guide for typographers and suppliers. The large number of packages involved in the project would have made it impracticable for the designers to prepare each item individually. On the other hand, all the firm's packages were to conform to the new design standard. The manual solves this problem; it is based on prototype designs of various sizes and proportions and permits easy setting up of individual packages in accordance with detailed specification sheets. General instructions, amply illustrated, serve to brief new suppliers or new company personnel on the constituent parts of the packages, including Federal regulations, production requirements and procedures, as well as specific design formulas. Although the designers continue to check packages in production, the manual cuts down the necessity for additional design consultation to a minimum, while at the same time it assures a high level of design throughout the hundreds of packages that make up the line.

Although the bulk of the packages fall into this standard but flexible design scheme, both the Cutter merchandising staff and Landor agreed on the desirability of providing separate design treatments for some pharmaceutical products, mainly hospital and over-the-counter items. These are sold for the most part under registered Cutter trade names, such as Enemol. For these items, the designers are developing individual designs that will differ from the uniform appearance of the regular line, yet be immediately recognizable as members of the Cutter family.



G. Barr & Company?

...never heard of them!

Probably not, son! But that aerosol tooth paste you and millions of other Americans are using today was very likely *private label manufactured* by G. Barr & Company in one of our two plants.

And while our name never appears on a container, G. Barr & Company's *aerosol packaging know-how* is the "hidden ingredient" that is helping to sell tens of millions of America's leading aerosol products today.

The hair spray, room deodorant, shaving cream, spray antiseptic, car polish, spray cologne and scores of other famous aerosol products found in homes all over America were in many instances developed in our research laboratories and private label manufactured by us.

Have you heard the G. Barr & Company story? Get the facts today.

G. BARR & COMPANY

Private Label Aerosols

3601 SOUTH RACINE AVENUE CHICAGO 9, ILLINOIS

Packaging and Selling

Industry Competition

One of the best examples of how competition between industries is in many ways becoming more important than competition by companies within a single industry was recently shown in Chicago.

In this city a Federal Saving and Loan Association put full-page ads in Chicago papers urging the public to keep their money in the bank and not to yield to the "buy now" durable goods promotions.

Copy in these ads said, "You're fed up with phony advertising, fake claims for the same old stuff, planned obsolescence. Hold on to your money until you are offered new things you can get some real satisfaction from at prices you consider reasonable."

In many ways this is questionable advertising and questionable business tactics.

At the same time, why should a business that depends on bank savings ignore, indeed yield to, another industry which is making an explicit drive to persuade its customers take their money away from the bank?

The soft goods industries went through a period in which certain heavy good industries, notably the automobile industry, were probably taking a great deal more than their share of the consumer's dollar by forced obsolescence, by glittering gadgets which raised the price and by other devices that went far beyond the thing they were suppose to sell, that is, the basic transportation of the automobile.

It is all very well for the automobile industry, which is paying richly for its own sins of both omission and commission, to stage hysterical drives all over the country: "You auto buy now." But if this means taking more of the consumer's dollar than is needed for automobile transportation, then it would be perfectly proper for other industries to fight back as vigorously and as bluntly as this bank is doing.

Declining Mailings

The torrent of direct mail that has been so harassing and disturbing to doctors and has worn out so many waste baskets is diminishing, according to one of the leading direct mail houses. This company has a checking system for measuring mail received by doctors which has been enforced for 15 years.

In the year ended April 30, reports this mail organization, mail volume dropped for the first time in the 15-year history of the survey. The Clark-O'Neill physician received 4,901 mailings during the year, compared to 5,041 in the previous year.

New Products

Lehn & Fink Products Corp. have joined that select circle of companies in this industry who are creating new products departments.

Dr. Thomas S. Harrison will head a new department devoted exclusively to the development of new products under the Lehn & Fink name.

Paying for Packages

Package designing has not quite reached the installment plan yet, but one leading package consultant, Alan Berni & Associates, has come up with the pay-as-you-go idea. That is, instead of paying with one big, fat check or with advance and a completion check, these folks are offering manufacturers a monthly payment plan.

Agency Switches

Well over 100 important advertising accounts switched advertising agencies during this spring's second quarter. Some of these switches have caused quite a bit of comment in advertising because no clear reason was given for the switch. Amid some of the most abrupt switches there is a general atmosphere of love and kisses which unquestionably is concealing quite a degree of unhappiness.

During this period Northam Warren Corp. moved its account of a little bit over $2,000,000 from J. M. Mathes, Inc. to Doyle Dane Bernbach.

In turn, Max Factor & Co. moved $3,000,000 out of Doyle Dane Bernbach, Inc. into Kenyon & Eckhardt.

Mennen Co. moved a reported $2,500,000 out of McCann-Erickson, giving $1,500,000 to Grey and $1,000,000 to Warwick & Legler.

Making no news at all, the Revlon account had some agency acrobatics.

Lanolin Plus took approximately $2,000,000 worth of billing from Kastor, Farrell, Chesley & Clifford to Erwin Wasey, Ruthrauff & Ryan. No saving on writer's cramp in writing checks in that switch.

Lanvin Parfums moved from North Advertising and split billings of something over $1,000,000 between Wesley Associates and Dowd, Redfield & Johnstone.

Meritseal... a capful of glamor

Your prestige cosmetic products deserve Crown's distinguished Meritseal closure. Meritseal's tasteful lithography commands attention in the showcase. On your high-speed production line, Meritseal caps spin on smoothly. Their precision-made threads assure easy removal and re-sealing. And there are no problems of expansion, contraction or cracking. Made in sizes from 33 to 100 mm.... with the right kind of liner for your product, all with special Meritseal "lock-in" construction.

for cans • closures • crowns • machinery CROWN

CROWN CORK & SEAL COMPANY, INC. 9300 Ashton Road, Philadelphia 36, Pa.

Lehn & Fink Products Corp. very abruptly moved $1,000,000 worth of Tussy billings from Grey to Young & Rubicam.

To Sell the Supermarket

Here again is an expert's opinion on the qualities your product needs to get into the supermarket. This is from Sidney R. Rabb, chairman of the board of the 90-unit Stop & Shop supermarket chain.

Stop & Shop, according to Mr. Rabb, has established a number of merchandising rules to guide its selection of non-food items. According to these rules, such items should (1) lend themselves to self-service selling and display; (2) have a high repeat factor, with mass appeal and rapid turnover; (3) represent a small unit of sales, and be easy to carry out of the store and large enough to discourage excessive theft; (4) be staple with a minimum variety of colors, sizes and styles— no fashion merchandise; and (5) yield a better than average profit.

On the basis of these rules, Stop & Shop are allocating about 15 per cent of the shelf space of all non-food products.

Super Sales

Here is a survey from the Super Market Institute: Health and beauty aids, the pioneer non-foods category and the perennial best seller, are now stocked by 98 per cent of SMI members markets. This is a 3 per cent gain over 1956.

The average number of items carried in this department are 325.

New Barber Group

Those of our readers who are interested in the barber shop market may want to make note of the newly formed Texas Barbers Association, which is the only state-chartered organization of barbers anywhere in the country that is non-union but open to journeymen and shop owners as well as commission men alike. This is the Texas Barbers Association of Austin, Texas.

Nasty Competition

We hope that the fight now going on in California in baby foods does not spread to this trade. Some of the implications of this lusty battle could touch off a chain reaction in certain branches of the cosmetic business.

Gerber baby foods has largely dominated the Californian market with its tin packed food line. Beech-Nut has had less than 10 per cent share of this market and has been packing in glass.

Just recently Beech-Nut started the fight when it cut prices on its baby food line in California. Gerber and Heinz claimed that this was thumbing the nose at the Federal antitrust law's ban on territorial price discrimination, because they define the territory as east and west of the Mississippi.

Beech-Nut claimed that the cut was made to meet the area of competition of Gerber, which sells its baby food in tins. Gerber's retort to this was that the use of glass jars makes Beech-Nuts baby food a premium product not directly competitive with Gerber's tins.

It is the side issue of this struggle that is disturbing, rather than the legal question of territorial price-cutting or the fight between the glass jar and the tin. Beech-Nut claimed that Gerber's salesmen "remodel and rearrange retailer' baby food departments—and in so doing whenever possible physically limit the space accorded by the retailer to competitors' products and in particular to those of Beech-Nut and rearrange competitive products in a mixed-up fashion so that prospective purchasers cannot find what they want."

Beech-Nut further charged that Gerber's salesmen reshuffle Beech-Nut displays so that "items having a rapid turnover are placed behind slower-moving items on lower shelves or even in the retailer's storerooms."

Another allegation was that the salesmen tampered with the jars of their competitors' baby food so as partially to open jars to destroy their usefulness and to spill over and spoil the appearance of Beech-Nut's baby foods display in retail stores.

We have heard a lot about the return of competition, but this is certainly jumping with both feet into some pretty bad practices. Health and beauty product manufacturers who are getting deeply involved in supermarket distribution, please note.

Between the Lines

One of the leading advertising agencies in this country has been taking full-page advertisements to promote its services in a field in which here to fore it has not been distinguished.

This advertisement shows the picture of an attractive young lady and the statement that the said advertising agency creates more fashion advertisements than any other agency.

This was a somewhat startling statement to those intimately associated with fashion advertising, because nothing pointing in this direction had ever occurred to anyone in this industry before.

We suppose there are two ways of creating fashion advertisements. One is to specialize in this field, to have several clients there and to place their advertising in such limited circulation style magazines as *Vogue* and *Harper's Bazaar*. With an average circulation of 200,000 for each of these publications, the fashion campaign of several fashion clients might amount to only 20 or 30 million fashion advertisements.

On the other hand, it is perfectly possible to inject a fashion note into ads for a client or two scheduled for *Life* or *The Ladies Home Journal* and run into the tall millions in a very short time.

We are all for provocative advertisements as a way to stimulate reader attention, but we do think statis-

tics should not be the tongue-in-cheek kind when you are seeking to create confidence and respect.

How to Get a Boom

When a labor union attacks an industry for lack of salesmanship, that ought to be news. The Textile Workers Union of America are now doing precisely that.

The research official from this union declared that paper and plastic industries had captured markets from the textile industry. The loss of markets in the last 6 years, with improved production methods and economic factors, have caused 1,000 mills to close, making idle 300,000 workers, he said.

"New products will mean new jobs. We are not opposed to technological improvements. We know that our jobs are not safe as long as technical facilities are used. But in order to stand up under technological improvements we must have new products and new methods."

When both union and management begin to think this way in other industries, the American economy will certainly begin to hum.

New Diversification

We were highly interested to receive a folder from Lehn & Fink describing the use of Lysol to eliminate thrips in gladiolus bulbs.

Since we take a modest degree of pride in our gladioli, it was welcome news that such an easy, convenient method would knock out these ghastly little pests.

Our interest was further stimulated by this new diversification in use and possibly in distribution, of one of the standard disinfectants of our trade.

This may suggest to sales managers and other marketing executives that even the old and established product should be returned to the research department for re-examination for new uses and for new marketing exploratory work.

Private-Label Selling

We admit to a complete inability to understand just what the Justice Department is aiming at when it urges the Senate to hold hearings in an investigation of retail private brands.

Gimbel Bros., R. H. Macy, Sears, Roebuck and Montgomery Ward are among the companies cited as possibly scheming all sorts of wicked and nefarious things with their private-label products.

We know what the Justice Department is charging, but we still do not understand what it is trying to achieve.

For instance, the Justice Department charges that certain retailers are using private brands as a competitive technique against other retailers selling nationally branded items at fair-trade prices.

Mr. Bicks of the Justice Department admits, for example, that the Department has "insufficient data available of this private brand phenomenon." But he goes on to say, "I can, however, suggest a possibly profitable path for this subcommittee's inquiry. Thus, large department stores or mail order houses may well encourage manufacturers to fair trade nationally branded items—the only items which the small retailers can secure. At this time, such mass sellers may market their own private brands—substantially identical to nationally branded goods—at prices lower than fair trade markups for the nationally branded counterparts.

"The result could be to enable large retailers, by hampering their smaller competitors' ability to cut prices, to hold an umbrella over the market for their own private branded items."

This seems to us about the weirdest kind of gobble-de-gook that has come out of Washington in a long, long time.

So far as we know, from a pretty close acquaintance with this trade over a good many years, it is possible for a small retailer in one way or another to secure his own private label line. As a matter of fact, literally thousands of small drug stores have experimented, at one time or another, with items under their own brand. Just about the last thing in the world in which there is any monopoly is the opportunity for a retailer to go into the private label business, even on a very small scale, if he feels he has any ability to sell his own label.

On the other hand, the private label business of many large stores is predicated upon two very functional marketing trends.

The first trend is the wide-spread movement of most advertisers into larger and larger national advertising with an openly declared intention of taking all sales control of the product out of the retailers hands and retaining in their own, the manufacturer's, hand. In other words, to relegate the retailer to an automation position and to minimize his store individuality, his creative ability as a merchant and any degree of independence on his part in relation to advertised brands.

As part of this move, manufacturers, as they grow, have been spreading their distribution wider and wider, in this way diluting their distribution and minimizing the opportunity for a capable merchant to build a clientele on which he can depend for repeat business.

To the extent to which a retailer can identify his own private-label business in the public mind with value and quality, he gains a franchise position on at least some products in which he is master of his own destiny.

Another reason for private-label is that a great many manufacturers are using extensive national advertising to secure what they call a "franchise" on the consumer's mind. They have marked up the price of their product, sometimes abnormally above its ac-

PACKAGING COMMITTEE AT LEDERLE

With ethical drugs, there's no margin for error—either in product or package. At Lederle Laboratories Division, American Cyanamid Company, where "packaging" means specifying, buying and handling millions of containers every month, this nine-man committee has authority in a particularly complex area.

Lederle uses thousands of different types and sizes of containers, creating special problems of inventory, package engineering, mechanization, quality control and delivery. It is vital, the Committee recognizes, to work with suppliers who are dependable, knowledgeable, and specialists in their field.

Federal, one of the four largest makers of folding boxes, has been a Lederle supplier for many years. Perhaps our kind of experience can be an asset to your packaging committee also.

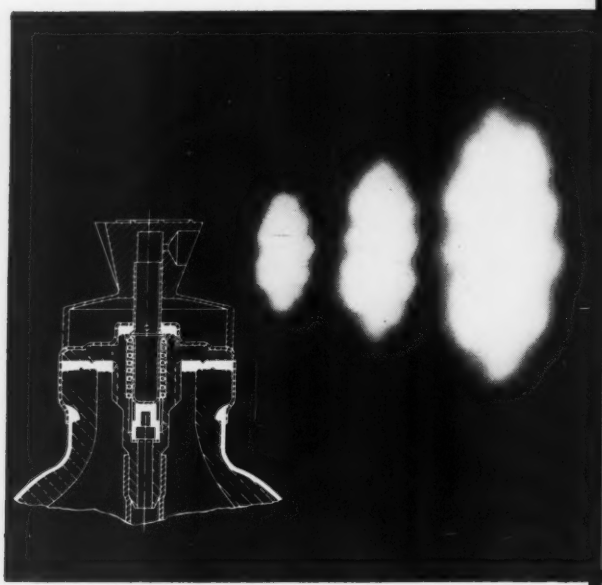
FEDERAL PAPER BOARD COMPANY, INC.

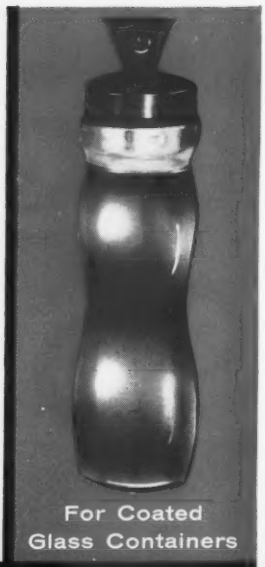
NATIONAL FOLDING BOX DIVISION • MORRIS PAPER MILLS DIVISION • EXECUTIVE OFFICES: BOGOTA, N. J.

OPERATING 16 PAPERBOARD MILLS AND FOLDING BOX PLANTS

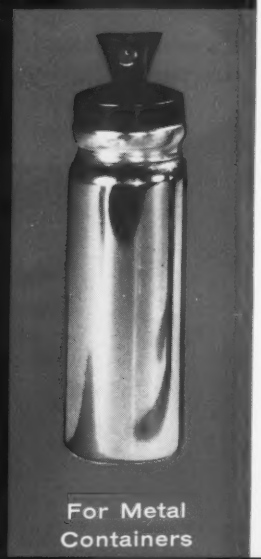
Creating New Horizons
In Cosmetic And
Pharmaceutical Packaging

RISDON METERED SPRAY AEROSOL VALVES

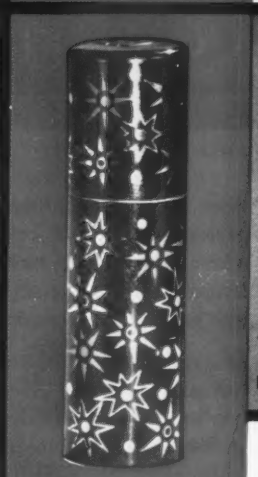




For Coated Glass Containers



For Metal Containers



For Combination Glass & Metal Containers

Available with Special Applicator-Actuators For Pharmaceutical Products

Creative research has made the Risdon metering valve another facet of Risdon's leadership in aerosol product dispensing.

You will find it in use on exquisite containers dispensing measured amounts of many of the best known perfumes. And in the pharmaceutical field, its ability to deliver the various pre-measured dosages desired, through special applicator-actuators, is opening new aerosol product possibilities.

It is available with either standard or patented Risdon "Micro-Mist" actuators, permitting unprecedented formulation latitude.

To serve your aerosol dispensing requirements Risdon offers technical advice and assistance plus extensive research, testing and quality control facilities and a fund of successful experience in the production of valves for a wide range of products.

For further information on Risdon metered-spray or conventional spray valves for glass, metal or plastic containers, contact Risdon today.

RISDON

THE RISDON MANUFACTURING CO.

Valve Division, Naugatuck, Conn.

RI-96

tual cost, in order to provide a very large sum for selling expansion.

This has provided a real competitive opportunity for certain capable retailers to offer a product that is comparable in quality to the national brand at a substantially lower price.

If we are to have a free American economy and a capitalistic, competitive system, it seems to us that the private label business must be recognized as being fully as legimate as any other way of doing business.

Growing Plastic Containers

Plastic bottles and tubes last year reached a production excess of 407 million units, as reported at the annual meeting of the Plastic Bottle & Tube Manufacturers Institute, a division of the Society of the Plastics Industry, Inc. According to the president of this institute, John Jennings, who is also sales manager of the Plastic Container Division of Continental Can Co., Inc., many factors have contributed to the continued growth of the industry. Growing consumer acceptance is, in part, due to product improvements stemming from new materials, flexibility of design and inherent advantages made possible by lower weight and handling safety.

Extensive research is being directed to an extension of the market for these containers. At the present time, by far the largest consumption is in cosmetics and pharmaceuticals.

Change

One way to prevent obsolescence in cosmetic products is to change the color. Apparently this is what Toni is doing with their present amber-colored hair shampoo. The new product, "Pink Pamper," will replace Amber Pamper. Of course, the product and the package are being changed, too.

Super Sales

The growth of supermarket sales for health and beauty products has certainly been a dynamic one during this last decade. There can hardly be any question that this branch of the retail trade has by now firmly established itself as a permanent part of cosmetic distribution. Granting this tremendous growth and present importance as a distributive outlet for cosmetics, it is nevertheless true that the supermarket still has certain very definite limitations as a retail outlet for our industry and probably always will have these severe limitations.

These limitations show up most clearly when we analyze supermarket sales product by product throughout this industry.

Recently, a very detailed analysis was made in a prominent chain which operates 37 stores. These stores, last year, did a total business of nearly $2,000,000 in the product of our trade. During this year the over-all business of this chain was slightly less than $80,000,000.

In this analysis it is extremely interesting to check the sales of health and beauty products for relative importance.

First, this department was divided into the following broad classifications. In the table below we give these classifications with the percentage of total sales and the number of items in that classification.

Item	*% of Total Sales*	*No. of Brands*	*No. of Items*
Dental needs	8.9	14	40
Drugs	29.1	79	138
Baby needs	4.0	15	27
Cosmetics	14.9	56	92
Hair needs	24.5	52	110
Shave needs	8.6	24	39

Here is the way the specific prdoucts that have a reasonable sales volume show up.

Product	*% of Total Sales*	*No. of Brands*	*No. of Items*
Toothpastes	16.7	7	23
Antacid	4.0	9	15
Laxatives	1.7	10	12
Headache remedies	7.6	6	15
First-aid	6.5	20	48
Face creams	2.7	7	13
Hand lotions	1.8	9	13
Hand creams	0.4	2	5
Colognes	0.3	2	2
Deodorants	5.9	12	25
Bath cosmetics	1.5	10	13
Face powder	0.2	1	4
Lipsticks	0.2	1	4
Shampoos	9.6	18	44
Hair dressings	5.9	10	19
Home permanents	4.0	7	20
Oils and tonics	3.2	10	17
Razor blades	3.4	5	9
Shave creams	3.4	11	19
After shave Preparations	1.3	5	8

This is a pretty clear-cut bookkeeping report of the kind of cosmetic business that is being done in grocery markets. It emphasizes the belief that the functional, staple, utility products of our trade are moving toward the supermarket, but that the style, prestige, glamour and fashion products have no place in this kind of a store.

New Package

A change in packaging, which dropped cartons to substitute cellophane, was reported to produce quite a substantial saving for the White Laboratories on their Cerofort Tablets.

In this new package six bottles are now tightly wrapped in cellophane without individual cartons. No sleeve, board or tray is required, and a paperboard divider separates the bottles, which minimizes shifting.

News in Packaging . . .

Rebuttal on Ocular Tests In Packaging Research

Louis Cheskin, Chicago marketing research authority, has replied to the report from the Center for Research in Marketing which called eye-movement testing "meaningless." Mr. Cheskin, who is director of the Color Research Institute of Chicago, states that his Institute has not claimed that eye-movement, visibility and readibility tests are means for discovering favorable or unfavorable meaning, but that they do reveal display effectiveness. Although visual effectiveness, which can be determined by an eye-movement test, is very important, it is not the whole story on the effectiveness of a package or an ad; the psychological effect of the whole must be tested also, and this is done in a field test conducted on an unconscious level with several hundred consumers.

According to Mr. Cheskin, the procedure for determining marketing effectiveness is comparable to the approach of a doctor: he first tests separate organs, then the functioning of the entire nervous system and psychological behavior.

New Anchor Hocking Warehouse

William V. Fisher, president, Anchor Hocking Glass Corporation, has announced the construction of additional warehouse space at the firm's Connellsville, Pa. glass container plant. It will provide 81,000 square feet of additional storage space.

Coppertone Suntan Lotion, manufactured by Plough, Inc., is now being packaged in a 2-ounce polyethylene tube that is unbreakable and spillproof. Made by Bradley Container Corp., a subsidiary of American Can Co., the tubes have a gloss finish to give added luster and reduce dust attraction. The new package retails for 69 cents.

Plastic Container Sales Up

One hundred thirteen million plastic bottles and tubes were sold during the first quarter of 1958, a 10.4 per cent increase over the number of units sold during the same quarter of 1957, according to the Plastic Bottle and Tube Manufacturers' Institute, division of the Society of the Plastics Industry, Inc. An increasing rate of growth is expected through the rest of the year.

The Institute ascribes this expanded use to the elimination of handling hazards as well as increased acceptance by the consuming public. Until now, the largest volume has been the smaller bottles and tubes used by the cosmetic and pharmaceutical industry, but the present trend indicates an increasing use of larger containers of polyethelene.

American Can Company Two New Presidents for

Kenneth M. Leghorn and Joseph D. Martin have been appointed presidents for two of American Can Company's wholly owned subsidiaries, according to William C. Stolk, president.

Mr. Leghorn, new president of Bradley Container Corporation in Maynard, Mass., who has been president of Sun Tube Corporation since 1953, succeeds Leonard A. Britzke. Mr. Britzke has been appointed general manager of the Canco division. Mr. Leghorn joined Sun in 1947 as an administrative assistant, later becoming assistant to the president and a vice-president.

Mr. Martin, new president of Sun Tube, which is located in Hillside and Washington, D.C., has been associated with that subsidiary since 1927 and has served in several capacities, most recently as executive vice-president.

P. D. Dilliard Named

P. D. Dilliard has been appointed to succeed R. F. Brenner, retiring director of Anchor Hocking Glass Corporation's chemical research and development laboratory, according to W. B. Snell, Jr., vice-president of the firm. Mr. Dilliard, who has been Mr. Brenner's assistant, joined Anchor Hocking in 1942, after six years with the Sharp-Schurtz Company in Ohio.

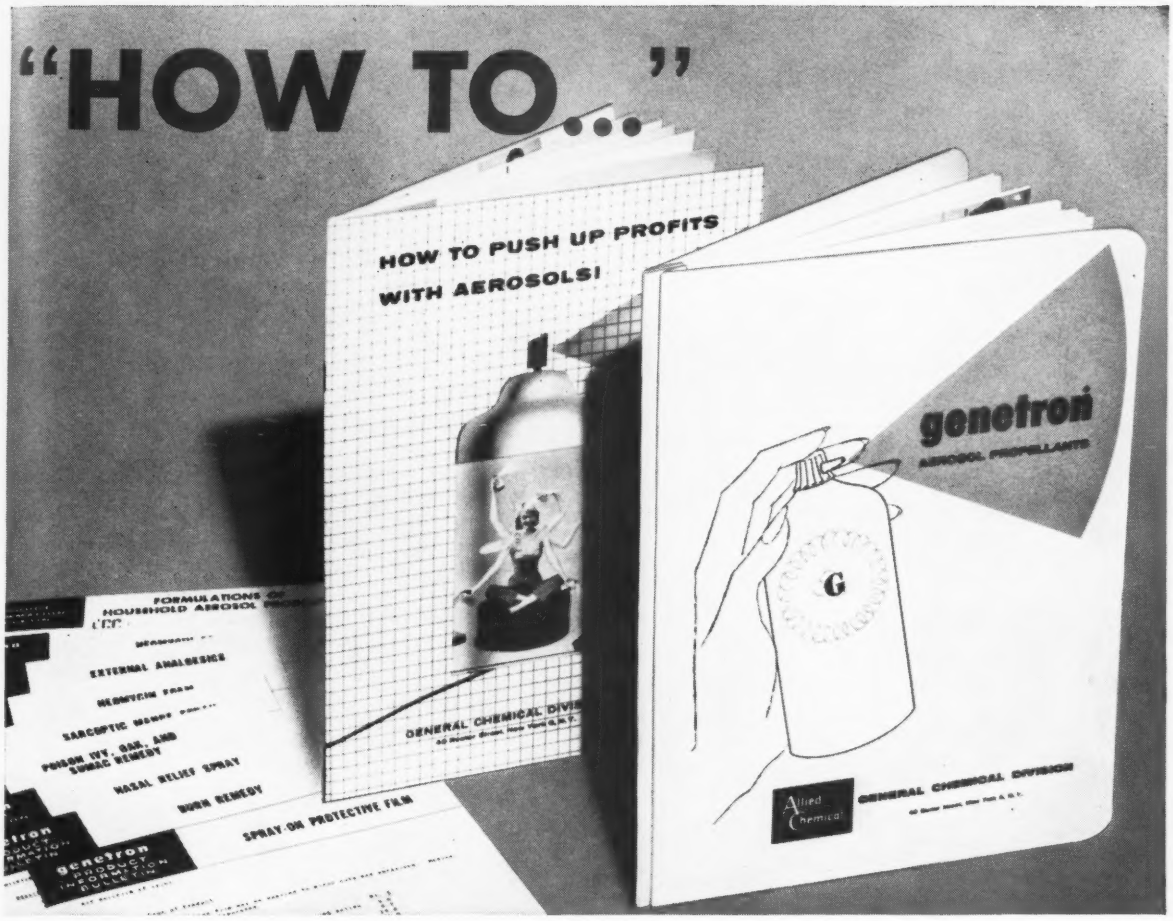
Max Factor's new deep-cleanser, Facial Bath, packaged in an easy-to-grip, nonslip bottle. The soft pink liquid, which can be seen through the container, makes an attractive contrast to the package lettering in garnet. A 3 and 1/8 oz. package retails for 69 cents, a 5 and 1/8 oz. package, $1.00, both plus tax.

Crown Cork & Seal Changes

William D. Wallace has been appointed director of manufacturing for Crown Cork & Seal Company, according to Karl W. Mueller, executive vice-president. Mr. Wallace joined Crown in 1957 as manager of industrial engineering, having previously served in similar posts with Continental Can Company and Chase Brass and Copper Company.

It has also been announced, by Daniel F. Sheehy, New York regional sales manager, that Jack P. Jordan has been named consolidated district sales manager for the firm in the New York area. Mr. Jordan has been with Crown for many years, most recently as New York assistant district sales manager and regional administrator.

New aerosol products available to consumers in Australia: Rilling Mystic Net (left) a spray-on hair net by Stock Affiliates Pty. Ltd., of Sydney for Rilling and Co., the New York-London firm, and Sombrero Sun Tan Lotion by Goya, of Melbourne. Both aerosols have valves and actuators by National Radiators, Ltd., Australian licensee of Risdon Manufacturing Company of Connecticut.



Free to aerosol marketers... helpful "how to" technical literature from General Chemical

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Describe promising new formulations and familiar tested ones for a variety of products studied or developed in our aerosol laboratory. Ask to be put on our mailing list.

☐ **How to Push Up Profits with Aerosols**

Contains valuable market and technical data... projections of potential sales in various markets, prepared by General Chemical's Market Survey Department . . . reliable sources for contract filling . . . basic information about aerosol packages . . . how aerosols work . . . outline of "Genetron" aerosol propellants.

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A technical manual which includes extensive data on the physical properties of "Genetron" propellants and mixes, General Chemical technical service, commercial filling methods, list of dependable contract fillers, and other topics of interest to the aerosol manufacturer.

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are putting the push in America's finest aerosols. All standard fluorinated hydrocarbon propellants and mixes are available in the full "Genetron" line—also special propellant mixes where unusual properties are required. Complete technical service is available from our aerosol laboratories.

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☐ *Product Information Bulletins*, and add my name to your mailing list.
☐ *How to Push up Profits with Aerosols*
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What is your choice in stock bottles? Tall, short, square, round . . . you'll find them all in the extensive Carr-Lowrey line. Here are our 338, 439 and C-39 styles. Decorated with your own design they make a package of which you can be justifiably proud.

GLASS STIMULATES SALES

CARR-LOWREY GLASS CO.

Designers and manufacturers of fine glass containers

Factory and Main Office: BALTIMORE 3, MD. — New York Office: 415 MADISON AVE. — Chicago Office: 1572 MERCHANDISE MART

D & C ADVERTISING NOTES

BY TED KLEIN, PUBLIC RELATIONS DIRECTOR*

AMA Newspaper

In a trade ad for the American Medical Association's tabloid, the AMA reports that 210,000 American physicians represent a potential market of over 3 1/3 billion dollars. That's what they earn annually according to the Association. The new publication, which is due in September, will be beamed at the doctor' broad interest in the world of medicine. It will accept "no advertisements that include claims pertaining to the health of people." AMA officials want to lure into the publication advertisers who have products that the physician will have to buy, rather than prescribe. The success of the tabloids prepared by Ciba, Upjohn and Lederle for physicians and dentists undoubtedly inspired the creation of *AMA News*. Editor is to be Jim Reed, long-time Kansas newsman. He will work out of AMA's Chicago office, with a staff of news reporters, not medical but "medically oriented."

Percentage of Sales and Advertising

Analysis of Internal Revenue figures shows that firms classified as producers of chemical and allied products spent about 3.31 per cent of their sales on advertising. Drug and medicine firms reported 5.98 per cent; perfumes, cosmetics and other toilet preparations, a high of 15.84. These figures are what firms report on their tax forms but may not actually represent a true picture of spending. It is interesting to note that of the 282 product or service classifications reported from more than 800,000 firms, cosmetics lead the list percentagewise in amount spent.

Toothpaste Advertising

Dentists are up in arms again on claims made by toothpaste manufacturers. Dr. Ralph Creig, member of the American Dental Association's Council on legislation has asked the government to pass a law to permit federal control of toothpaste advertising. He wants laws similar to FDA statutes, which would make advertisers submit medical proof of claims. "The burden of demonstrating the validity of therapeutic claims in advertising belongs morally, ethically and logically with the party asserting them" he insists.

Here is another example of how advertisers had a long warning before the dentists went to the government. Ad men in the industry have always known that dentists were antagonized by some of the claims in the toothpaste ads, but they were content to wait until the boom was lowered before they did anything.

The time for advertisers to get a story across is before the unpleasant light of government inquiry is shown on advertising and reflected on industry. Here is a chance for an industry conference, to see to it that claims would be documented.

AMA to Sponsor Medical-Pharmaceutical P.R. Meeting

Under the direction of Leo Brown, AMA Public Relations Director, a two-day Institute will be held in Chicago at the Drake, August 27-28. John Modrall (Lilly) heads the program committee. Basic information on how drug p.r. men and county, state and national AMA executives can work together will be presented. Any information for those who would like to attend can be obtained by contacting Leo Brown at the AMA in Chicago.

TV or Not TV

The notable lack of success in a network TV series on medicine has prompted a new tack in TV. New shows being readied for fall programming will concentrate on local news pick-ups, heart operations and other dramatic medical subjects. No one has been able to sell a drug company on sponsoring a new health series to the public. Whoever does come up with a formula that will help the physician, inform and entertain the public, yet will not stir up controversy, should have a fine public relations tool.

In the June 1st issue of the Canadian Medical Association Journal, an editorial calls attention to U. S. citizens' preoccupation with "their bodies and minds." It discusses the increasing number of appearances on TV by American physicians. It has some interesting points of contrast with the Canadian and U. S. medical thinking.

11 Drug Firms Doing Anti-Cancer Drug Research

Over $3,500,000 has been allocated to top drug companies to test effectiveness of compounds that can control cancer. Schering, Merck, Armour, Pitman-Moore, Bristol, Upjohn, Parke Davis, Squibb, Abbott, Pfizer, Hynson, Westcott & Dunning and recently Syntex (Mexico) are listed by the National Cancer Institute. With such tremendous public interest, these firms will have their public relations hands full if and when they ever hit pay-dirt. A notable example of how this sort of research under a spotlight can end up, was the polio vaccine story, recently climaxed by a federal indictment. A public information campaign at the beginning of this sort of a project could very possibly result in a better environment when a product is marketed. A continual liason with the press *during* the course of investigation could have them on the side of the industry when the big story breaks.

*Paul Klemtner & Company, Inc.

A PACKAGING TEAM NEEDS

To get the best packages for their products, more and more companies are making packaging decisions *team* decisions. But a packaging team isn't complete unless it has the "outside" viewpoint – the kind of viewpoint you get from an Anchor Man!

The Anchor Man is a glass packaging specialist. He's helped solve hundreds of tough packaging problems, and he can help solve yours through this wide experience.

He offers a complete line of Anchorglass® containers – amber, crystal and green – in all standard sizes and styles. The quality of these containers is safeguarded by hundreds of daily checks, tests and controls. You get the same high quality standards in the complete line of Anchor®

AN ANCHOR MAN!

metal and molded closures. And you get container-closure combinations that are best for you in every way.

Contact your Anchor Man. We know you'll like his service. We know you'll want him on your team, too. Anchor Hocking Glass Corporation, Lancaster, Ohio. Branch offices in all principal cities.

ANCHOR HOCKING

Glass Containers and Closures

Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

The Patent System as a Stimulus to Competitive Effort in Research and Development

It is doubtful whether very many people ever stop to think that the patent system actually fosters competition. The chances are that 99 out of 100 people, or maybe the ratio is even higher, would state that the patent system is a means for avoiding competition. Both views would be correct, depending on just what is meant by competition.

Normally one thinks of patents as being helpful in obtaining a monoply, for example, on a new product, and thereby avoiding competition. This is the usual sense in which the patent system is considered as operating. However, there is a very wide view which is, incidentally, held by this writer, that the patent system has the very healthy effect of fostering competition, namely, in new ideas. In this manner, it is felt that the patent system operates to bring about a far greater amount of research and development than would occur in the absence of such a system. A strong argument for this view is contained in Study No. 2, prepared for the Subcommittee on Patents, Trademarks and Copyrights of the Senate Committee on the Judiciary, by George E. Frost, a Chicago patent lawyer. Actually, Mr. Frost considered the impact of the patent system on the modern economy in much broader terms than those of its effect on research and development. However, we are here concerned only with the latter rather narrow question.

A close look at Mr. Frost's report is in order.

First, as already indicated we are dealing with competition in the conception, development, application and marketing of new products and processes. It is Mr. Frost's thesis that the patent system "provides a protected market with the opportunity for unusual profit necessary to justify the heavy investment in time, effort and capital necessary to bring the improvement to the public. This same protected market provides an entering wedge by which a business enterprise entering a new field can overcome the obstacles that otherwise discourage entry into an industry already populated. Finally, the ever-present threat of new firms with exclusive rights to new technologies compels existing enterprises to explore avenues of improvement upon pain of sudden obsolescence. All of these effects aid in generating a dynamic progressive environment under which the businessman must compete not only in terms of production and sales technique but must also exert his talents in the direction of technological improvement."

There are many forms in which the patent system operates to stimulate product competition. It permits a newcomer to challenge the established members of an industry. Royalty-supported research organizations are compelled to continue their developments or otherwise perish through loss of income. Also, the established manufacturers are forced into this competition of ideas in order to maintain or improve their positions, or avoid the expense of royalty payments. Then too, the patent system helps the individual inventor by reason of the competition it engenders among his prospective manufacturing customers, for each of them realizes that if it closes its doors to ideas from individual inventors it may be kept out of a promising development.

Mr. Frost goes into considerable detail in his report in documenting his thesis. One example that he uses is the field of color television. It appears that the two principal patent licensing organizations in the industry are RCA and Hazeltine. RCA is supposed to have invested $65 million in color TV research as of the date of the report (1957). Hazeltine has concentrated on color TV research during the last six years with an annual expense for this item of approximately $1 million. Neither company has yet received any significant return on this investment. Furthermore, each faces the competition of other organizations.

Another instance of competition in development mentioned by Mr. Frost is that of coal-mining machines. The coal industry had fallen behind general economic growth, due mainly to increased labor costs and the competition of oil and gas. Today the situation is quite different, largely due to research in the mining and utilization of coal. Development has been marked in the area of machines that attack and remove solid coal in underground mining.

Development of the coal mining machines also illustrates the manner in which competitive research and development generates its own chain reaction of activity. Machines now available break loose the coal more rapidly than it can be transported to the surface. The result is a competitive race to devise new machines for transporting the coal. The industry looks to patent protection for the fruits of its research and development in order to cover the investment.

One of the earliest examples of competitive research and development is that of the oil refining industry. At first, petroleum refining was little more than a simple distillation process producing kerosene as the principal product and, as a nuisance byproduct, gasoline. When the demand for gasoline increased before World War I, it was realized that it could not be satisfied by the simple distillation methods then available. The result was the development of the thermal cracking process. This in turn led to the organization and maintenance of research laboratories by the various major petroleum refiners, and to the organization of independent research and engineering companies serving the small refiners. The next major development in the petroleum field, that is, the catalytic cracking process, occurred just prior to World War II. One of the results of this development was that the U. S. A. and its allies had 100 octane gasoline available, in contrast to the Axis powers, who were largely con-

*Richards and Cifelli, Newark, New Jersey

With Bernardin · Quality is a **SERIES** of satisfactions

STEEL

A metal closure is made of steel. The die that stamped it out is made of a different steel. The tool that made the die is of a still different steel. Many of the steels come to us ready for use and require only check testing. Others, like the high-carbon, high-chrome steel we require for certain tools, are tempered in our furnaces and hardened to our own standards.

Pictured here, the hardness of a die is being tested. In the background a blank from that die is checked for accuracy.

At Bernardin, nothing is taken for granted. Thus, with steel, as with all production phases, each operation and the product of that operation is under continuous control with one purpose in mind. To produce millions of closures, each of which expresses "Quality" in all the functions required of it.

QUALITY METAL AND PLASTIC CLOSURES BY

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fined to gasoline of about 87 octane rating.

Competitive research continues today in the petroleum refining industry. A number of competing catalytic cracking processes have been developed. Developments in reforming, alkylation and other processes have taken place. Indeed, research in petroleum has created a new industry, the manufacture of petrochemicals. These products made from petroleum are useful as raw materials for plastics, synthetic rubber, synthetic fibers and detergents. Present plant investment is said to be in excess of 4 billions of dollars and is rapidly rising.

A well-known example of competitive research is that furnished by the drug industry. The field of antibiotics may be mentioned. Penicillin is in the public domain. The development of streptomycin in 1944 by Dr. Waksman at Rutgers in conjunction with Merck was a milestone in the antibiotic field. Merck chemists then developed dihydrostreptomycin. Parke, Davis developed "Chloromycetin." Changes in the fields of antibiotics come thick and fast. The competition is fierce. Research moves ahead quickly. Then, almost before one knows what is happening, someone comes up with another antibiotic, and the whole cycle starts all over again. The research scientists are continually under pressure to develop new drugs and improve existing ones.

An example of the help the patent system gives the newcomer is that of Thiokol Chemical Corp. This firm was founded in 1925 to manufacture the synthetic rubber developed by Joseph C. Patrick. The patent rights made it possible for Thiokol, in spite of its small size, to build on this new development and expand considerably. An unexpected dividend of research on Thiokol has been that it has become very important for use as a rocket propellant.

Mr. Frost says that industries such as the antibiotics and synthetic chemicals industries would undoubtedly carry on even in the absence of a patent system, but that the research would be on a secret basis. Mr. Frost feels that the pace of activity would be slowed and what he calls "cross-fertilization" between competing research efforts would be impeded. Without a patent system it is difficult to believe that there would be as much immediate publication of research results as exists today. Since each new devlopment plants the seeds of thought in the minds of others, it is obvious that operating on a secret basis would be harmful.

Other examples of the patent system enabling the so-called small person to obtain a foothold in industry would include those of Clarence Birdseye (frozen foods), P. R. Mallory & Co. (radio components) and Polaroid Corp. (photography).

Perhaps the whole subject has been nowhere stated better or more succinctly than by Federal Judge Evans in 1942 when he wrote:

"The patent system encourages invention, not only in that it rewards the inventor with a patent, but it spurs the competitors to put forth their mightiest effort to produce a product as good, yet different from the patentee's. . . . It must be admitted that in an effort to avoid infringement of a patent, as much skill is often displayed as is shown in the conception or development of invention itself. There is, however, nothing objectionable in this. In fact, it is thus that the patent system is working at its best. For it is then that we have competition between a holder of legal monoply and his competitors. It illustrates how the legal monopoly evidenced by a patent excites the competitors to their best, to meet or excel the product covered by the existing patent. Competition among industrial rivals and inventors is thus incited."

That the view of Mr. Frost has some dissenters cannot be denied. Indeed, the same committee that sponsored Mr. Frost's report has recently announced that another report prepared for it and entitled "The Impact of the Patent System on Research" comes to the opposite conclusion. This report was prepared by Seymour Melman of the Department of Industrial Engineering, Columbia University. Professor Melman's study deals with the increasing emphasis upon cooperative research conducted by large industrial and university research laboratories.

"As a foundation for his analysis," Senator O'Mahoney said, "Professor Melman examined the patent policies of several such laboratories and in the light of these inquiries explored the role of patents as a stimulus to invention, in shaping the direction and extent of research, and in accelerating or retarding the disclosure of research information. After examining the correlation between research and patenting, Professor Melman concludes that, in these areas of research at least, the patent system contributes little to the progress of science and useful arts."

Odor Characterization Apparatus

R. W. Moncrieff, a well-known English writer in the field of perfumery, recently obtained U. S. Pat. No. 2,837, 912 on an apparatus for the characterization of odors. The patent has been assigned to Airkem, Inc. It is recommended reading to everyone in the field of odor evaluation, for it not only contains a wealth of information but also is written in Mr. Moncrieff's usual interesting manner, only slightly impeded by the need to conform to patent terminology and practice.

Briefly, Mr. Moncrieff's appartus involves the use of at least 3 adsorption tubes each having different adsorbent material. Air is mixed with the odorant under test, passed through the tubes at such a rate that the air after it passes through the tubes can be sensed as containing a definite odor. The rate at which the air is passed through the tubes is used as a gauge of the critical time of adsorption for the odorant with respect to the particular adsorbing media. As a result, the apparatus permits the assignment of numbers to characterize the adsorption properties of the odorant.

While Moncrieff states that a weakness of the various known approaches to the characterization of odors has been primarily the subjective nature of these approaches, depending upon the sensitivity of the nose and the differences in olfactory sensitivity in individuals, and the problem of olfactory fatigue introducing complicating factors, nevertheless, the nose still plays some part in the utilization of Moncrieff's apparatus. This is so because the end point in each case is reached when the smell of the odorant material is unmistakably recognizable at the outlet.

Nevertheless, Moncrieff's apparatus does appear to give an objective and quantitative measure of the different behavior of odors with respect to the adsorbent materials employed. He admits that the careful stand-

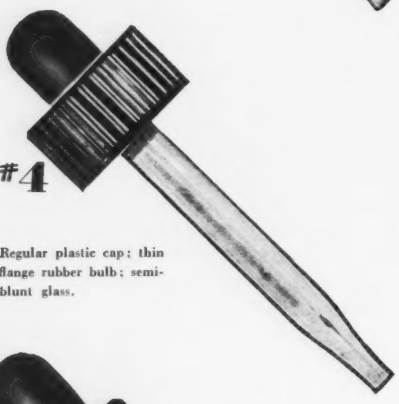
(*Continued on page 226*)

NEW PERFECTION
DROPPING PARTS
meet EVERY
"Satisfaction Test"

QUALITY	A-1
UNIFORMITY	A-1
PERFORMANCE	A-1
CLEANLINESS	A-1
SERVICE	A-1

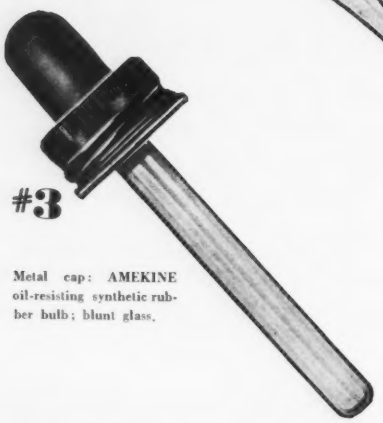
#1

Non-rolling, extra-depth, Bakelite cap; thick-flange rubber bulb; Saftee-ball glass.



#4

Regular plastic cap; thin flange rubber bulb; semi-blunt glass.



#3

Metal cap: AMEKINE oil-resisting synthetic rubber bulb; blunt glass.

They're A-1 with your customers, too . . . assuring you repeat sales!

When you sell a product that pleases and satisfies your customers, you're assuring yourself of their goodwill and continued patronage. New Perfection Dropping Parts help to give you that kind of a product. They are convenient, attractive, dependable—manufactured and assembled under careful and constant inspection to assure the highest possible quality.

RUBBER BULBS are supplied in many styles and colors. Oil-resisting AMEKINE synthetic rubber is used for oil preparations; natural rubber is supplied for other products.

CAPS of plastic or metal can be furnished in a complete range of sizes and colors.

DROPPER GLASSES are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

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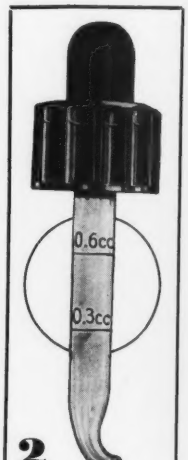
We can make up dropping parts to fit your own bottles or we can supply bottles in an attractive modernistic style in Amber, Blue, Green, or Clear glass, complete with dropping parts, in the following sizes: 1/8, 1/4, 1/2, 1 and 2 oz.

• • • • •



2

Non-rolling extra-depth Bakelite cap; thick flange rubber bulb; special bent glass. (Calibrated in color).

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"Glass Goods of the Better Kind"

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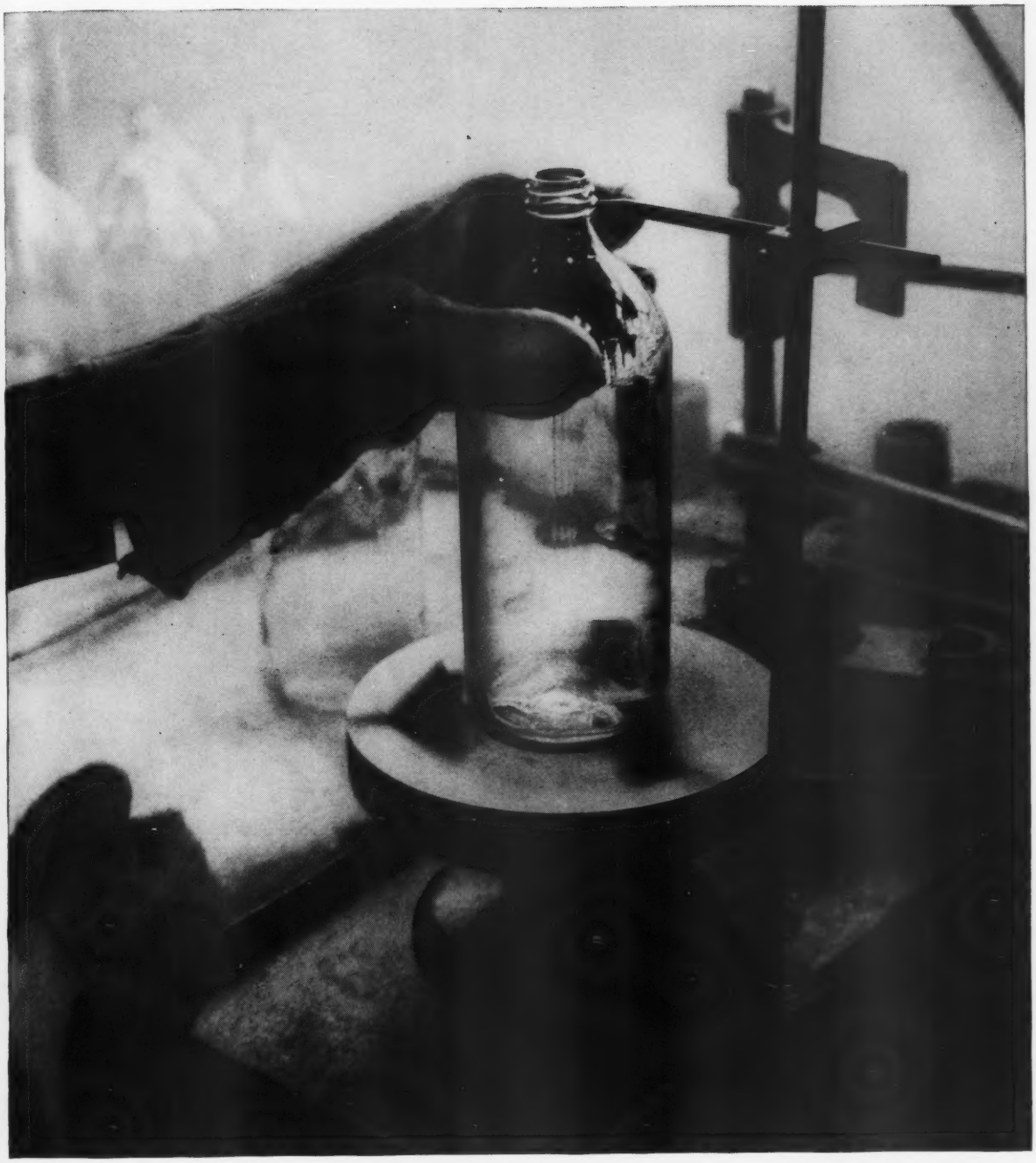

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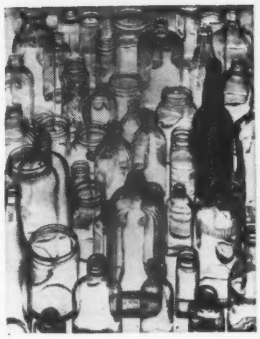

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This new packaging idea dominates a $70,000,000 market

Introduced just four years ago, aerosol-packaged colognes now account for more than half of total cologne sales. Aerosol packaging has taken command of this $70,000,000 market and has also revolutionized sales for hair fixatives, shave creams, insecticides and a host of other products.

Sales records and marketing data prove the appeal of aerosol packaging. In a recent market survey, housewives who tried aerosol cologne preferred it 6 to 1 over any other form. The reason: aerosol cologne is easier to use and apply, and there is no waste or evaporation.

If your product can be brushed, poured or sprayed, you stand a good chance to add new appeal—create a positive competitive advantage—if you packaged it in an aerosol.

It's surprisingly simple and inexpensive to put the unique advantages of aerosols to work for you. A custom filler near you has the specialized knowledge and equipment to help you. He can package your formulation for testing and help you from planning through production.

* * *

If you don't know the name of a custom filler, write Du Pont. We'll send you a list and include survey data on your market for colognes plus information about Freon* propellents for aerosols. More of today's successful aerosols are powered with "Freon" than with any other propellent. Write E. I. du Pont de Nemours & Co. (Inc.), "Freon" Products Division 348, Wilmington 98, Delaware.

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*FREON AND COMBINATIONS OF FREON- OR F WITH NUMERALS ARE DU PONT'S REGISTERED TRADEMARKS FOR ITS FLUORINATED HYDROCARBON PROPELLENTS

NEWS...

New Associate Director for Merck Institute for Therapeutic Research

Dr. Bettylee Hampil has been appointed associate director of the Merck Institute for Therapeutic Research, according to an announcement by Dr. Maurice R. Hilleman, Director of the Merck Institute. Prior to her recent appointment, Dr. Hampil served as director of virus research of the Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc.

BETTYLEE HAMPIL

Dr. Hampil began her association with Sharp & Dohme, Inc. in 1936, first working in the anaerobic laboratories, then in the Technical Division as a bacteriologist. With the organization of Sharp & Dohme's Medical Research Division in 1940, she was appointed head of virus and rickettsial research. Under her guidance the department first developed Rocky Mountain Spotted Fever vaccine and antiserum.

During World War II, Dr. Hampil's department was active in developmental research on effective vaccines for diseases against which vaccines were not available. The group was responsible in large degree for the development of typhus, influenza and Japanese encephalitis Type B, vaccines.

Dartell's Executive Vice-Pres.

Paul Wickman, former director of public relations for Schering Corporation, has been named executive vice-president of Dartell Laboratories—biochemical (manufacturing and research) with headquarters in Los Angeles.

Pitman-Moore Names M. E. Daniels

Mitchell E. Daniels has been named marketing coordinator for Pitman-Moore Company, it was announcer by Stewart E. Ruch, vice-president in charge of sales.

MITCHELL E. DANIELS

Mr. Daniels joined the pharmaceutical firm as a medical service representative in 1951. For the next five and one-half years he represented the company in the Bristol, Tennessee, area before being named Charlotte, North Carolina, district manager, a position he held for 15 months.

Fritzsche Elects Officers and Directors

At the annual meeting of the stockholders of Fritzsche Brothers, Inc., New York, held early in July, the following were elected directors of the company: John L. Cassullo, Frederick H. Leonhardt, Jr., Ernest Guenther, William H. Mathers and Ellis F. Merkl.

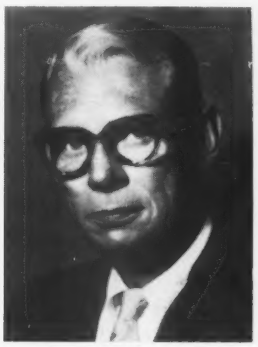
Following the stockholders meeting, the annual meeting of the board of directors was held, and the following officers were elected: John L. Cassullo, president; Frederick H. Leonhardt, Jr., vice-president; Ernest Guenther, vice-president; Edward E. Langenau, vice-president; Ellis F. Merkl, secretary and treasurer; A. J. Hemminger, assistant secretary; and E. C. D'Andrea, assistant treasurer.

Bezard Returns to States

Louis Bezard, president of De Laire, Inc., accompanied by his wife, recently returned by plane from a six-week trip to Europe where he visited Portugal, Spain and France. In France he spent some time in Issy les Moulineaux, where he conferred with the directors and staff of the parent company.

Revlon Appoints Two

Charles Revson, President of Revlon, Inc. has announced the appointment of William D. Mewhort to the newly created position of executive vice-president of administration and operations for Revlon and its subsidiaries. Before his appointment at Revlon, Mr. Mewhort had been vice-president and treasurer of Textron, Inc., and its subsidiaries since 1949.



GEORGE C. KIRK

Mr. Revson has also announced the appointment of George C. Kirk as vice-president in charge of sales. Until his appointment, Mr. Kirk was associated with International Latex Corp., most recently as vice-president of sales for the Playtex Division.

Recent Pfizer Appointments

The recent appointment of Robert D. Newton as assistant director of operations research for Chas. Pfizer & Co., Inc. has been announced. Formerly a senior analyst, Mr. Newton joined Pfizer in 1946 as a production supervisor at the chemical and pharmaceutical firm's Brooklyn plant. Assigned to the production headquarters staff in 1950, he transferred to operations research in 1957.

Pfizer has also announced two appointments to its Chemical Sales Division: Robert D. Knoebel and Carl Lorentzen. Mr. Knoebel, formerly on the staff of the food and beverage department, has been promoted to field sales manager for the eastern region of the division. He joined Pfizer in 1952 as a sales representative in the mid-west region upon graduation from Notre Dame University.

Carl Lorentzen was appointed to the staff of the Chemical Sales Division's industrial department. Formerly an eastern region sales representative, Mr. Lorentzen joined Pfizer in 1954.

thurification

n. (Latin, Thurificati, worshippers who appeased the gods with gifts of incense)
To perfume or make fragrant.

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Barley and Mitzner Join van Ameringen-Haebler

It was recently announced by van Ameringen-Haebler, Inc., that Ralph C. Barley has been appointed manager of the company's Engineering Department. Mr. Barley was formerly senior process project engineer at American Cyanamid Company in Bound Brook, New Jersey, and previously he was associated with the Foster Wheeler Company and the General Aniline and Film Corporation in similar capacities.

The company has also announced that Bernard M. Mitzner has been appointed supervisor of the Instrumental Analysis Section of the company's Analytical Department at Union Beach, New Jersey. In this new post Mr. Mitzner will coordinate and supervise the use of instruments for the analysis of raw materials and finished products. The company has been using infrared and ultraviolet spectroscopy as well as gas liquid chromatography and is presently investigating new instrumental techniques that may become useful analytical tools.

Mr. Mitzner was formerly with Lederle Laboratories, before which he was a member of the staff at Columbia University, where he was engaged in instrumental analysis research. During his service in the United States Army he worked on infrared and ultraviolet analysis techniques at the Army Chemical Center in Maryland.

Wyeth International Names Pazery

Paul H. Pazery has been appointed assistant advertising manager of Weyth International Limited, according to Robert C. Hodgman, president.

For the last eight years Mr. Pazery has been a member of the international advertising department of Smith Kline & French Laboratories, Philadelphia. Previously he was employed by A. P. de Sanno, Inc., Phoenixville, Penna.

A native of England, Mr. Pazery was educated in that country and in France. He first came to the United States in 1939 while serving on the staff of the French Ministry of Foreign Affairs. After becoming an American citizen he served in the U. S. Navy from 1943 to 1945, with the Office of Strategic Services in Washington and with Naval Intelligence in Oran Algeria.

Vanderbilt Co. Names Two

The R. T. Vanderbilt Company Specialties Department, which produces and markets chemicals for the cosmetic, pharmaceutical and agricultural trades, has announced two appointments to its field sales staff:

JAMES DENNIS NOLAN

THOMAS M. KUGEMAN

James Dennis Nolan, of Norwalk, Conecticut, who will cover the midwestern states west of Chicago, and Thomas M. Kugeman, of Westport, Connecticut, who will cover the midwestern states east of Chicago, and the Province of Ontario.

Bristol Labs Appoints George M. French

The appointment of George M. French as assistant to the sales manager of Bristol Laboratories has been announced by Richard A. Anderson, vice-president and director of marketing. For the past sixteen months Mr. French has been regional manager for the southeast and southwest with headquarters in Memphis, Tenn. His new post will bring him to Bristol's New York City offices.

Mr. French joined Bristol Laboratories as a professional representative in 1946 immediately after his discharge from the U. S. Navy. He is the founder of the company's Dallas and Memphis districts.

Organon Appoints New Division Chief

Organon Inc. has announced the promotion of Joseph Palmaccio to the position of chief of the company's Sterile Products Division. Prior to joining Organon, Mr. Palmaccio had served in supervisory and research capacities with E. R. Squibb and Sons, and was assistant to the chief of the Sterile Products Division of Organon before his promotion to his present position.

JOSEPH PALMACCIO

R. Gaines Promoted

Robert C. Gaines was recently promoted to the post of director of sales training in the Wm. S. Merrell Company, according to an announcement by Frank N. Getman, president. With Gaines' promotion the company plans to emphasize further the importance of sales training in improved promotion and dissemination of information on products of Merrell research to the medical profession.

Mr. Gaines has spent most of his business life in the drug industry, primarily in chain store operation. He joined Merrell as sales representative 14 years ago, was later advanced to district manager, then promoted to head up Merrell's merchandising activity in Cincinnati, and then assistant sales manager.

Union Carbide Chemicals Reassigns Representatives

The transfer of four technical representatives was recently announced by Union Carbide Chemicals Company, division of Union Carbide Corporation.

The transfers are: Lory A. Crisorio to the Chicago district; D. Wallace Enright to the Charlotte district; H. Robert Hubbs to the Indianapolis district; and Bernard W. Hurley to the Chicago district.

Atlas Powder Announces Major Personnel Changes

The board of directors of Atlas Powder Company has announced several major personnel changes, including the election of the firm's president, Ralph K. Gottshall, as chairman of the board in addition to his re-election as president. As chairmain of the board Mr. Gottshall succeeds Isaac Fogg, who is retiring this month after nearly 46 years of service. Mr. Fogg will remain as a director, member of the finance committee and chairman of the committee on audit. The board also announced the election of Edward J. Goett, senior vice-president, to the position of executive vice-president.

RALPH K. GOTTSHALL

EDWARD J. GOETT

Other changes announced included: Edward J. Massaglia, general manager for operations of the chemicals division, elected vice-president and general manager of the newly consolidated chemicals division. Robert J. Reilly, assistant treasurer, elected treasurer and secretary, succeeding Preston W. Parvis, who also is retiring this month after more than 47 years of service (Mr. Parvis remains a member of the board and has been appointed a member of the committee on audit); John H. Leary, assistant to the president, elected assistant treasurer and assistant secretary; Norman E. Miller, company controller, elected an officer.

Officers re-elected were vice-presidents James R. Frorer, Charles C. Gammons and William C. Lytle; and Arnold J. Fiedler was re-elected assistant treasurer and assistant secretary.

EDWARD J. MASSAGLIA

Mr. Fogg joined the Atlas treasurer's office when the company began operations in 1913. He had served formerly as secretary and purchasing agent of the Goshen Iron Company in Virginia, and as secretary to Professor Edwin J. Houston, one of the inventors of the Thompson-Houston Arc Light, from 1902 to 1906. After serving Atlas as assistant treasurer, then treasurer and director, he was elected vice-president in 1931, and president of the company in 1945, which position he held until his election as chairman of the board in 1953.

Mr. Gottshall was appointed by Atlas as a chemist in 1927. He shifted to sales work after eight years of production and supervisory experience at Atlas explosives plants, becoming director of explosives sales and later assistant general manager of the explosives division. He was elected vice-president in 1951, executive vice-president in 1952, and president in 1953.

Mr. Goett joined Atlas as director of what was then the commercial development department, in 1954. He was elected a member of the board and vice-president in charge of the chemicals division and chemical research the same year, and senior vice-president in 1957. He had formerly been a member of the board and manager of sales development for Chas. Pfizer & Co.

Mr. Massaglia joined Atlas in 1955 as assistant general manager of the chemicals division, becoming general manager for operations of that division in 1956. He was formerly administrative vice-president and a member of the board of Pfizer International, Inc.

Walker Appoints Pendrak

Joseph F. Pendrak, formerly field sales manager, has recently been appointed assistant general sales manager for Walker Laboratories, Inc. Mr. Pendrak has been with the company since 1948, serving as detail representative, supervisor, division manager, and, finally, as field sales manager, prior to his recent promotion. His new responsibilities involve a sales expansion program in connection with the firm's current growth.

Two Join Webb & Co.

As part of its current expansion prgram, R. D. Webb & Co., Inc. of Cos Cob, Conn., manufacturers of food flavors and essential oils, have appointed R. E. Beaumont, Beaumont Brokerage Co., P. O. Box 232, Bellevue, Washington, as north-western representative, and George A. Hart to its Chicago sales staff.

Mr. Beaumont will cover the states of Washington and Oregon, Mr. Hart, the state of Illinois.

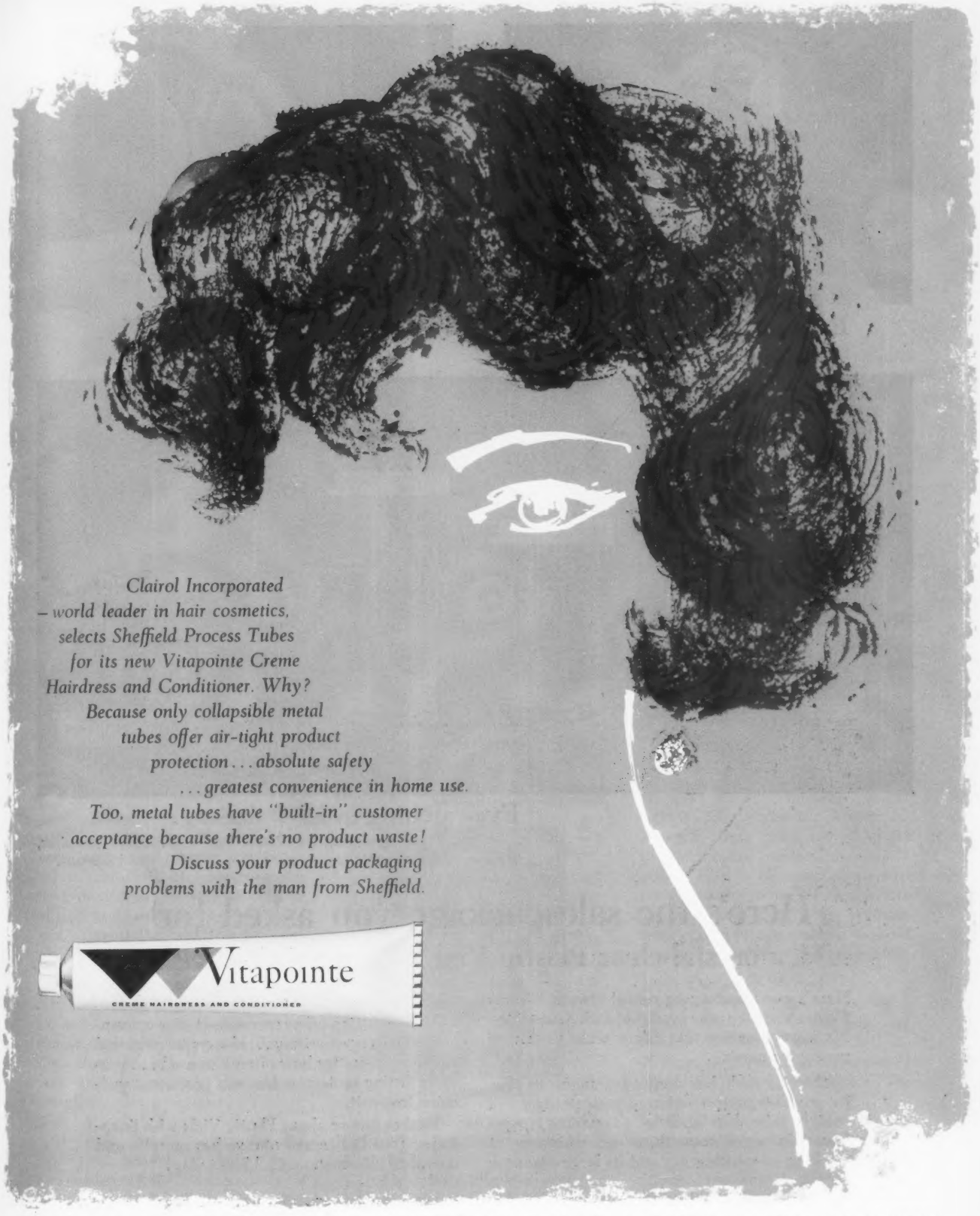
William Barlow Honored

William H. Barlow, a founder and charter member of the American Society of Perfumers, Inc., recently received the 1958 Pratt Alumni Medal from Pratt Institute of Brooklyn, N. Y., in recognition of his more than 40 years of service to the alumni and the Institute.

The citation, which was presented by Robert F. Oxnam, president, stressed Mr. Barlow's services in founding the Pratt Institute Alumni Federation, which coordinates the alumni activities of the five schools comprising the Institute. He has also served as chairman of the Science and Technology Alumni Council.

Mr. Barlow retired in 1956 after 9 years as first secretary of the American Society of Perfumers, at which time he received a $500 bond in appreciation. He is now chairman of the by-laws committee.

Mr. Barlow is director of the perfume research laboratory of Orbis Products Corporation.



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– world leader in hair cosmetics,
selects Sheffield Process Tubes
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Hairdress and Conditioner. Why?
Because only collapsible metal
tubes offer air-tight product
protection . . . absolute safety
. . . greatest convenience in home use.
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acceptance because there's no product waste!
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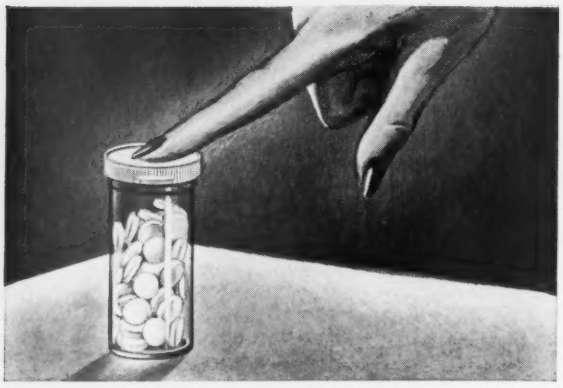
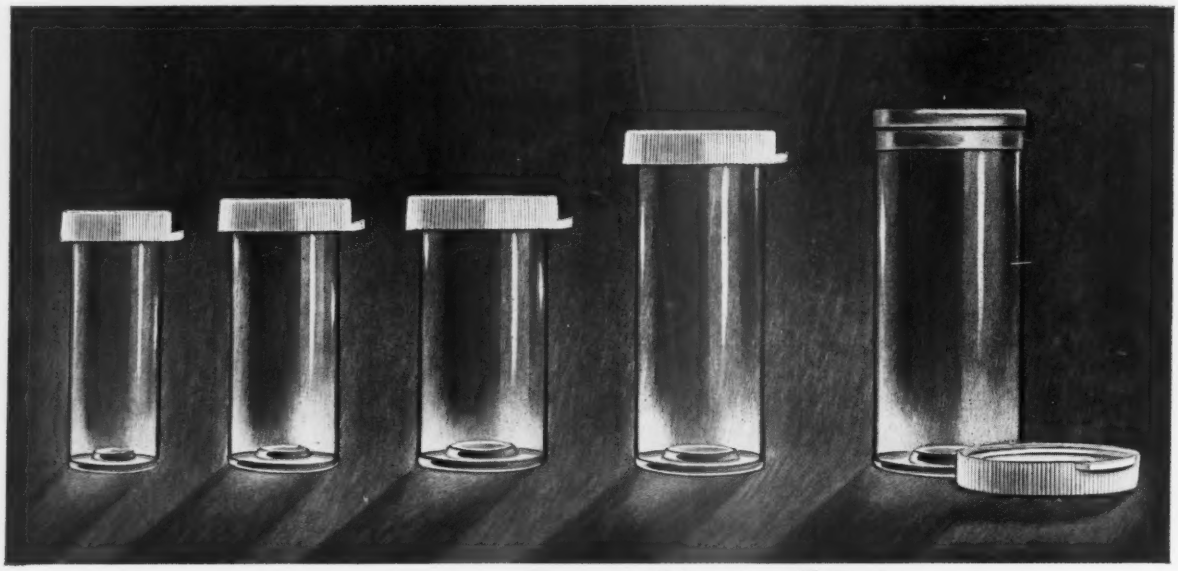
Easy off . . .
Snap-Caps pop off crisply!



Easy on . . .
Snap on tightly no matter how often used!



Eye-catching in all 7 sizes . . .
Trim, attractive—new Snap-Cap Plastic Vials are available in 7 sizes, with these approximate capacities: 1, 3, 5, 7, 9, 13, and 15 drams.

Here's the salespackage you asked for–
a crystal-clear Plastic Vial with a SNAP-CAP!

Here's good packaging news! Owens-Illinois Plastic Vials are now available with SNAP-CAPS. It's a combination that fills a wide variety of packaging needs.

The vial, itself, has many advantages: its clarity provides perfect vision of your product . . . straight sides ease labeling . . . opening is reinforced for extra strength, added resistance to cracking or splitting . . . and its large-diameter opening speeds filling . . . eases removal, too.

The Snap-Cap offers unmatched user convenience: Pops open *crisply* . . . always snaps closed *tightly*—no matter how often it is used . . . provides lasting protection for your product at welcome low cost.

Find out more about Plastic Vials with Snap-Caps. Your O-I representative has samples and complete information. Call him today!

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AN (I) PRODUCT

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GENERAL OFFICES • TOLEDO 1, OHIO

Changes at White Labs

The election of K. A. Bartlett as vice-president, production, for White Laboratories, Inc., was recently announced by James C. DeCesare, president of the firm. Mr. Bartlett, who joined White Laboratories in 1930, had been director of operations prior to his new position, and he is also assistant treasurer of the company.

K. A. BARTLETT

DAVID J. MORRISON

The promotion of David J. Morrison to production manager has also been announced. Since coming to White's in 1946, Mr. Morrison has been named successively as director of packaging, of shipping and traffic and of receiving and warehousing.

Bierwirth, Coppedge Elected

John E. Bierwirth, president of National Distillers and Chemical Corporation since 1942, was elected chairman of the board, and Roy F. Coppedge, Jr., an executive vice-president since 1957, was elected president, at a recent directors' meeting.

Mr. Bierwirth has been a director since 1942, prior to which he served as president of the New York Trust Company. Mr. Coppedge, until 1953 a partner of Breed, Abbott & Morgan, general counsel for National, joined the firm as vice-president that year.

Dorothy Sked Named Roche Librarian

Dorothy A. Sked has been named research librarian for Hoffmann-La Roche Inc., according to an announcement by Dr. John A. Aeschlimann, vice-president in charge of chemical research.

Mrs. Sked was formerly assistant professor of library science of Montclair State College. She has also served as librarian of the College High School at Montclair State, librarian of the Thomas Jefferson Junior High School, Fair Lawn, N. J., and as a research librarian for Allen B. Du Mont Laboratories.

T. Waugh Honored

Theodore Waugh of Fritzsche Brothers, Inc. Aerosol Laboratories, who completed twenty-five years of service with the New York essential oil and chemical firm this month, has been made a member of the Fritzsche Quarter-of-a-Century Club.

At a luncheon in his honor, Mr. Waugh was presented with a substantial government bond and a scroll by the officers and board of directors, together with a gold wrist watch, appropriately engraved, from the firm's employees. He is the seventy-third Fritzsche employee to be so honored.

MacFarlane Promoted by Lilly

John O. MacFarlane has been selected by Eli Lilly and Company for the newly created post of assistant director of biological development.

JOHN O. MACFARLANE

For the last five years Dr. MacFarlane has been head of the biological development department, directing a unit dealing with new biological products and improving existing products and methods.

Dr. MacFarlane joined Lilly in 1948 after receiving his Ph.D. from the University of Cincinnati.

ADOLPH DINGFELDER

Dingfelder Named President of Reynaud

Adolph Dingfelder was recently made president of Reynaud Ltd., manufacturers of essential oils. Mr. Dingfelder has been in the essential oils industry for many years.

New Sales Positions At Parke-Davis

The appointment of seven men to new assignments within its U. S. sales organization has been announced by N. L. Yarbrough, manager of U. S. sales operations for Parke, Davis & Company.

The appointments are: Donald P. Hayes, from sales representative to field manager in the company's Los Angeles branch; James D. Hill, from sales representative to field manager in the Kansas City branch; Richard A. Kolb, from sales representative to the hospital medical service division; Harold W. Pace, from sales representative to field manager in the Kansas City branch; Arthur C. Scherrer, from sales representative to the hospital medical service division; John L. Summers, from sales representative to the hospital service division; and David H. Webster, from sales representative to field manager at the New Orleans branch.

Janet Devanney Named

Janet Myers Devanney has been appointed advertising and publicity director of Colonial Dames, Inc., according to a recent announcement by H. P. Willats, president of the cosmetic company.

Mrs. Devanney will work in conjunction with Victor Pearson, recently promoted to the post of merchandising promotional manager, and Jerry Dalebout, who has recently assumed the position of general sales manager. Mrs. Devanney was formerly publicity director of Bourjois, Inc., New York.

Colonial

DROPPERS AND ASSEMBLIES

Stress—

* Q.F.

THE Quality Factor, "Q.F.", in Colonial droppers and assemblies plays a key role in giving mothers peace of mind. Colonial's painstaking attention to quality standards has produced a product which continually meets modern hygienic demands required for new arrivals.

Let our technicians make free samples to your exact specifications. We have a Special Services Department to provide precision calibration in silk screening and hot stamping, too. It will pay you to contact a Colonial representative listed below or write to us directly.

Packaging Institute's
20th Annual
National Packaging Forum
Oct. 13, 14, 15, 1958
Edgewater Beach Hotel
Chicago, Ill.

Specialists in Glass or Plastic Droppers and Assemblies for Nearly a Quarter of a Century.

Represented by:

CHARLES E. SCHWAB
122 E. 42 St.
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OXford 7-0760

ALLEN J. GRETSCH
327 LaSalle St.
Chicago 4, Ill.
WAbash 2-1619

HARRY M. GRABER
811 S. 53rd St.
Philadelphia, Pa.
GRanite 6-6311

GABLER & GABLER
435 S. LaCienega Blvd.
Los Angeles 48, Cal.
BRadshaw 2-2995

RICHARDS GLASS COMPANY
102 Atlantic Ave.
Toronto 3, Canada
LEnox 2-3311

COLONIAL APPLICATOR CO.

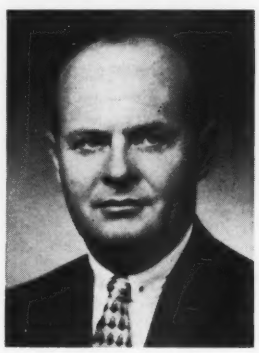
VINELAND, NEW JERSEY

Hobson and Mullally Named by E. R. Squibb

E. R. Squibb & Sons, division of Olin Mathieson Chemical Corporation, has announced the appointment of Lawrence B. Hobson as medical director of the division, and Walter E. Mullally as assistant manager of the veterinary department.

LAWRENCE B. HOBSON

Dr. Hobson joined the company in 1949 as an associate medical director and has been medical director of the international division since 1954.



WALTER E. MULLALLY

Mr. Mullally first served Squibb in 1936, in the San Francisco branch office, and later as professional service representative and in sales, on the West Coast.

Kessler Expands Facilities

Kessler Chemical Company, Inc., Philadelphia, has recently opened its second manufacturing plant at Cottman Avenue and State Road. According to Dr. W. B. Pings, general manager, this new facility doubles plant capacity and provides improved production units for glycerol monostearate, synthetic waxes, surface active agents and other fatty derivatives. Kessler Chemicals doubles production facilities.

British Cosmetic Chemists Meet

The tenth annual general meeting of the Society of Cosmetic Chemists of Great Britain was held on May 16 in London, with over 80 attending.

Retiring president J. Pickthall presented the report of the council for the year. Highlights were the visit of 35 members of the Society of Cosmetic Chemists U.S.A., which strengthened the good will existing between the two societies; seven extremely successful meetings have been held; the courses at Brunel College of Technology, Acton, have resulted in eight more students receiving the society's diploma; membership has increased by 28, to 283; and arrangements are now being made for the British Congress of Cosmetic Science in April, 1959.

Mr. Pickthall took the opportunity to plead that the "veil of secrecy" be lifted by employers, noting that too often lectures could not be arranged because prospective lecturers could not obtain employers' permission.

Officers elected were: president, R. H. Marriott; vice-president, H. W. Hibbott; hon. secretary, P. A. Lincoln; and hon. treasurer, R. E. Spate. Three members of the council were chosen: S. J. Bush, R. T. Dobson and J. B. Wilkinson.

An informal dinner celebrating the tenth anniversary of the society's formation followed, at which F. V. Wells, a honorary member of the society, was guest. Mr. Wells introduced Mr. Pickthall, who recalled that the meeting that resulted in the founding of the society, at first as a chapter of the American society, had been at Mr. Wells' instigation. Mr. Wells, in his reply, said that credit was due also to other founding members, in particular, M. G. deNavarre and Walter Taylor, S.C.C. (U.S.A.).

European Administration Office Established by Shulton, Inc.

The formation of a new European administration office in New York to coordinate all European activities has been announced by David Gregg, Jr., vice-president of Shulton, Inc.

John H. Douglas has been named manager. He formerly served as general manager of the firm's subsidiary in Leiden, The Netherlands, to which position Hans H. Gottmer succeeds. Mr. Gottmer was formerly assistant general manager.

Cannon Joins Northam Warren

Gerry Cannon has been appointed assistant general manager of the Northam Warren Corporation, according to an announcement by Northam Warren, president of the firm.

GERRY CANNON

For more than 22 years Mr. Cannon has been associated with Lehn & Fink Products Corporation, where he served in various executive capacities. He formerly served as account executive for Dorothy Gray with the advertising agency Kenyon & Eckhardt.

In his new position Mr. Cannon will work closely with Northam Warren, Jr., vice-president and general manager of the corporation.

Nancy Chilson's Nose Knows

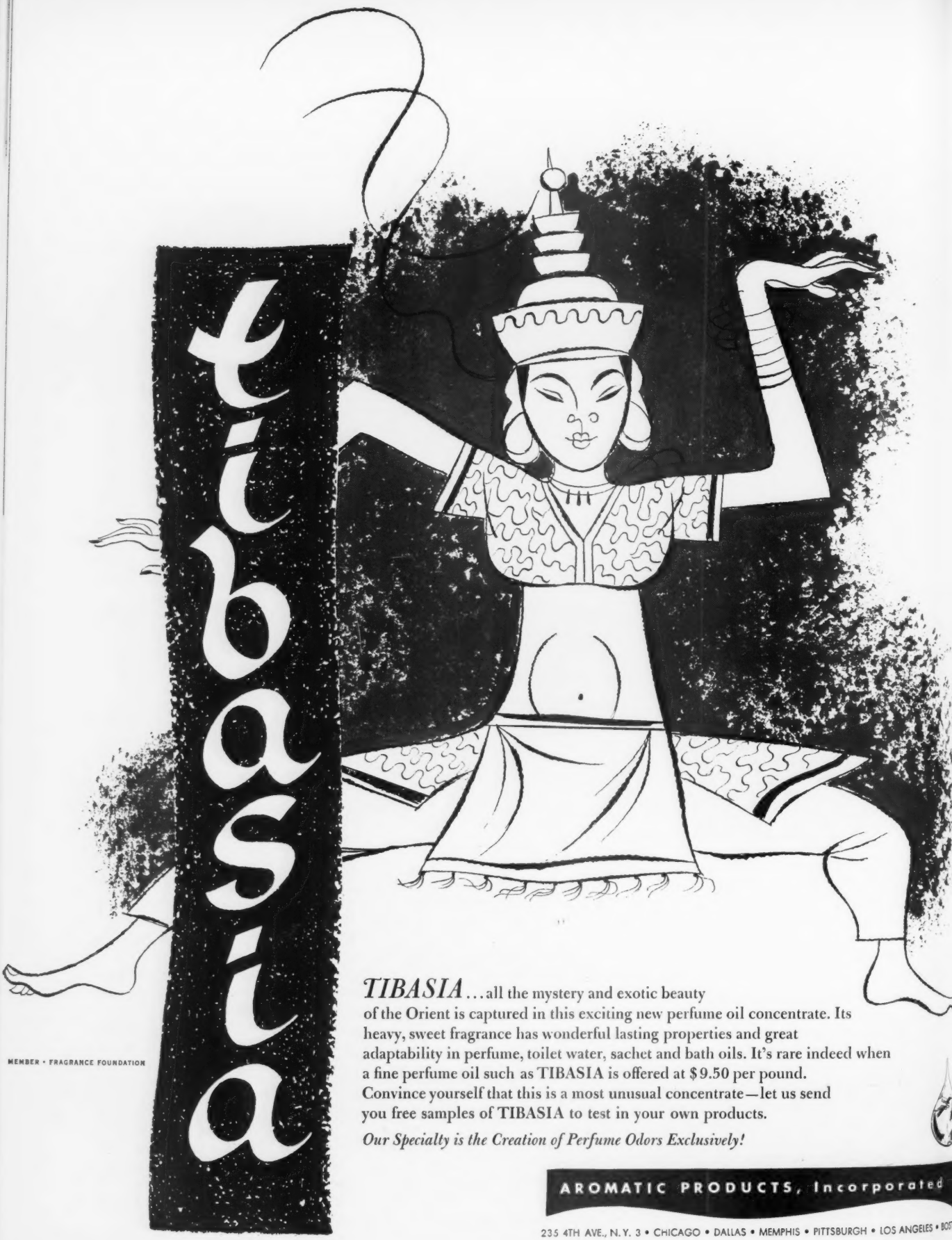
A recent issue of the *New York Herald Tribune* carried an account by Marilyn Mercer of Nancy Chilson's work as a member of a three-man perfume evaluation board at van Ameringen-Haebler, Inc., manufacturers of essential oils and perfumes.

Miss Chilson, daughter of Francis Chilson who writes our Management Forum each month, began as a medical laboratory technician and research assistant, then chose to work with scents.

Her department's primary purpose is to choose scents that will help sell products—household items such as detergents, medium-priced cosmetics and shoe and car polish. The board also evaluates fine perfumes.

Fritzsche Brothers Changes Address

Fritzsche Brothers, Inc., is now located at 5537 N. Clark Street, Chicago 40, Ill; the new telephone number is LOngbeach 1-9271-2-3-4; and the warehouse is at 5474 N. Elston Avenue, Chicago 30.



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TIBASIA... all the mystery and exotic beauty of the Orient is captured in this exciting new perfume oil concentrate. Its heavy, sweet fragrance has wonderful lasting properties and great adaptability in perfume, toilet water, sachet and bath oils. It's rare indeed when a fine perfume oil such as TIBASIA is offered at $9.50 per pound. Convince yourself that this is a most unusual concentrate—let us send you free samples of TIBASIA to test in your own products.

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PERFUME OIL CONCENTRATE FOR PERFUME, TOILET WATER, SACHET, BATH OIL

George Denton Beal Retires

George Denton Beal is retiring as a director of research at Mellon Institute on August 31, after 32 years of service.

Dr. Beal has had a notable career in chemical research, pharmaceutical investigation and education and research management in a number of industrial fields, including textiles, paper, leather, waxes, varnishes and food chemistry. He has many publications to his credit.

Dr. Beal has received the Ebert Prize and the Remington Honor Medal from the American Pharmaceutical Association, and the Pittsburgh Award of the American Chemical Society in 1955.

Dr. Beal has held major offices in the American Chemical Society, the Pennsylvania Chemical Society, and the American Pharmaceutical Association. He is president of the American Council on Pharmaceutical Education, and a member of the Board of Trustees of the convention which prepares the Pharmacopeia.

Dispergent Co. Changes Hands

Walter A. Taylor has announced the purchase of the Dispergent Company from the founder, Charles T. Maeding.

In line with Dr. Taylor's plan for expansion, the company has been moved to a new plant in Guilford, Connecticut, where enlarged manufacturing and research facilities have been completed. Mr. Maeding remains with the firm as associate.

The Dispergent Company produces specialized emulsifiers, dispersants, and solubilizers for the cosmetic, pharmaceutical and chemical specialties industries under the trade name of Neocol.

Dr. Walter A. Taylor, new owner of the Dispergent Co. (left) and Charles T. Maeding, founder, opening company's new laboratory and plant at Guilford, Conn.

Bryant Pharmaceutical To Open New Plant

David Schwartz, president, Bryant Pharmaceutical Corporation, has announced the imminent completion of its new two-story plant at 70 MacQuestin Parkway South in Mount Vernon, N. Y.

The new building, which consists of 25,000 square feet of floor space, adjoins the main lines of both the New York Central and the New York, New Haven & Hartford railroads. It will house facilities for the manufacture and processing of a complete line of pharmaceuticals, and the plan includes a unique automation technique for handling liquids in such a way that they are never exposed during the manufacturing process.

Occupancy of the new building is expected in early October, according to Jerome Berk, vice-president of the company.

Little League Baseball Field Dedicated

At a recent ceremony dedicating a Little League baseball field which van Ameringen-Haebler, Inc. provided on their property adjacent to the firm's Union Beach plant, a certificate of appreciation was awarded the company by Philip J. Cassidy, president of the Union Beach Little League Association.

The ball park is located near Highway 36 on a portion of the company's 150-acre tract housing the research and chemical processing operations of the perfume and flavor manufacturer.

Parenteral Drug Assoc. Announces Annual Convention

The Annual Convention of the Parenteral Drug Association, Inc. will be held at the Hotel Statler in New York City, on October 22, 23 and 24.

The convention will consist of three days of scientific papers pertaining to parenteral drug manufacture and marketing, as well as the medical aspects of injectibles. There will also be exhibits by suppliers of material for this industry.

A more complete program will be announced at a later date. Program arrangements are being made by Dr. Harold Blumberg under the guidance of the president, William S. Bucke of Lafayette Pharmacal, Inc.

Upjohn Board Changes

Mrs. Donald S. Gilmore has resigned after 33 years of service from the board of directors of the Upjohn

ROBERT M. BOUDEMAN

Company, and Robert M. Boudeman has been elected to fill the vacancy.

Mr. Boudeman, associated with Upjohn since 1940, has worked primarily in the firm's international operations. In 1956 he was made assistant director and in 1958 executive vice-president, both of Upjohn International Operations, Inc.

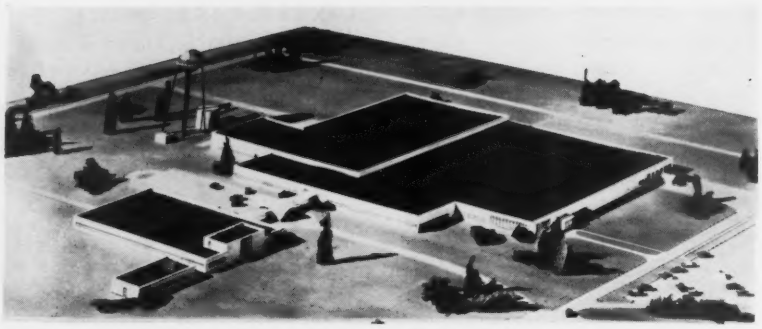
Abbott Laboratories Forms Biological Control Dept.

New assignments and the organization of a new department in the scientific divisions of Abbott Laboratories have been announced by Elmer B. Vliet, vice-president and scientific administrator.

A new Biological Control Department will be formed in the Control Division to centralize control functions using biological methods. Dr. Harry E. Sagen has been named manager of the department and Dr. Allen P. Saunders, assistant manager.

Appointed to succeed Dr. Sagen as manager of production quality control was Lester A. Feiertag. Dr. Hugh Vincent will transfer to the Production Quality Control Department, and Harvey S. Miller will take over the work of product quality review formerly in charge of Dr. Vincent.

The Microbial Physiology Department has been organized into two sections. Dr. Waldo C. Friedland was named head of the section on microbial metabolism and development. The other section, microbial genetics and assays, will report directly to the department head, Dr. Merlin H. Peterson.



Architect's scale model of Carter Products' new plant in Cranbury, N. J. to be completed in 1959. Wigton-Abbott Corporation, Plainfield, N. J. are the architects and builders.

Carter Products Builds New Plant

Carter Products, Inc. began construction in Cranbury of a $3.5 million plant, its second in New Jersey, as Governor Robert B. Meyner turned the first shovel full of earth at the 150-acre site. Completion of the building is slated for late summer, 1959.

The new plant will include manufacturing, shipping and warehouse facilities for all Carter toiletry and proprietary products, as well as for those of its pharmaceutical division, Wallace Laboratories.

The Cranbury facility, which was designed and will be constructed by Wigton-Abbott Corporation of Plainfield, is a one-story structure and will occupy approximately 250,000 square feet of floor space. Most operations will be air conditioned. The plant is expected to employ about 300 persons.

Waverly Purchases Industrial Site

Waverly Chemical Company, an affiliate of the Robinson Wagner Company, Mamaroneck, N. Y., has contracted to purchase a fifteen-acre industrial site on the eastern shore of the Hudson River near Phillipstown, New York. The property has riparian rights to the river and access to an unlimited supply of water. The main line of the New York Central Railroad passes by its western boundary.

The new facilities are scheduled to be completed and in operation by the late spring or early summer of 1959. A comprehensive line of surface active agents including emulsifiers, dispersants, penetrants and wetting agents for cosmetic, pharmaceutical and industrial use will be produced. William B. Jerome, vice-president of Waverly, will be in charge of the operation.

Kohnstamm Expanding

H. Kohnstamm & Company, Inc., has announced plans to move its executive offices from Park Place to 161 Avenue of the Americas, New York City, tentatively early this fall. The new offices will include two floors offering skylight laboratories and about 30,000 square feet of working space.

Paul Kohnstamm, president, has announced, further, that the Kearney flavor plant is to have an addition that will add 20,000 square feet of floor space and almost double production of flavoring extracts when completed this November.

The work is under the supervision of David Jorysch, technical director of the flavor department, who was recently elected assistant vice-president of the company.

Scores Hole in One

Robert Horsey, vice-president, Givaudan-Delawanna, Inc., recently scored the first hole in one during the 26 years of the BIMS Golf Tournaments, at the Winged Foot Golf Club, Mamaroneck, N. Y.

Canco Opens Sixth Coil Installation

American Can Company recently added another link to its nationwide network of coil processing facilities with the dedication of a 90,000-square-foot plant in Los Angeles, the sixth opened in the last 18 months by the firm.

The new facility, adjoining Canco's can-making plant, shears giant coils of tin plate and steel plate into standard can-making sheets. It has a capacity of more than 90,000 tons of plate a year.

Two more such installations will be opened later this year.

John Johnston

John L. Johnston, who retired in 1949 as president of the Lambert Company, parent concern of the Lambert Pharmacal Company and other subsidiaries, died July 14 at his home in Cape Vincent, New York.

Since Mr. Johnston's retirement, the Lambert Company has become part of Warner-Lambert Pharmaceutical Company. Mr. Johnston also served as a director of the Continental Can Company, among many others.

Arthur Jacks

Arthur G. Jacks, vice-president and treasurer of Adolph Gottscho, Inc., Hillside, New Jersey, died on July 11.

Martin Straus

Martin L. Straus II died July 17 at Lenox Hill Hospital in New York City. Mr. Straus was president of Bymart-Tintair, Inc., hair-coloring producer, which he founded seven years ago.

Dr. Hamao Umezawa of Tokyo University, discoverer of the new antibiotic kanamycin (left), is greeted upon his arrival at New York International Airport by Dr. Philip I. Bowman (center) and Dr. Amel R. Menotti of Bristol Laboratories, which developed and tested the drug. Dr. Umezawa is one of several Japanese scientists who attended the recent conference on kanamycin held at the New York Academy of Sciences, New York City.

Rosottones... essences elite

now from Penick

Popular Rosottones are now included in the long line of essences offered by Penick. Like the stately rose itself, Rosottones recall the natural rose fragrance. Rosottones remain stable in all oils and are available in three price ranges, providing you with flexibility and good value.

ROSOTTONE* SUPREME

The aristocrat of rose essence . . . unique in its approach to the Bulgarian otto. Very powerful and long-lasting, it is suggested as a partial replacement for natural oil in all types of perfumes.

ROSOTTONE

Rosottone is enhanced by the natural rose undertones. It maintains excellent stability in all blends for use in cosmetics.

ROSOTTONE SAVON*

This specialty offers the famous Rosottone character in a form suitable to soap and detergent perfumery. Ideal stability in laundry and liquid soaps of all types. It will not discolor cosmetic creams and is particularly recommended for use in oil-in-water type products.

With its modest price, ROSOTTONE SAVON opens a new field for manufacturers desiring a "natural" rose effect.

We will be happy to send samples of all three ROSOTTONES. Simply attach the coupon to your letterhead.

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735 W. DIVISION ST., CHICAGO 10

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Gentlemen: Please send a sample of
Rosottone Supreme Rosottone Rosottone Savon

Name:_____ Title:_____

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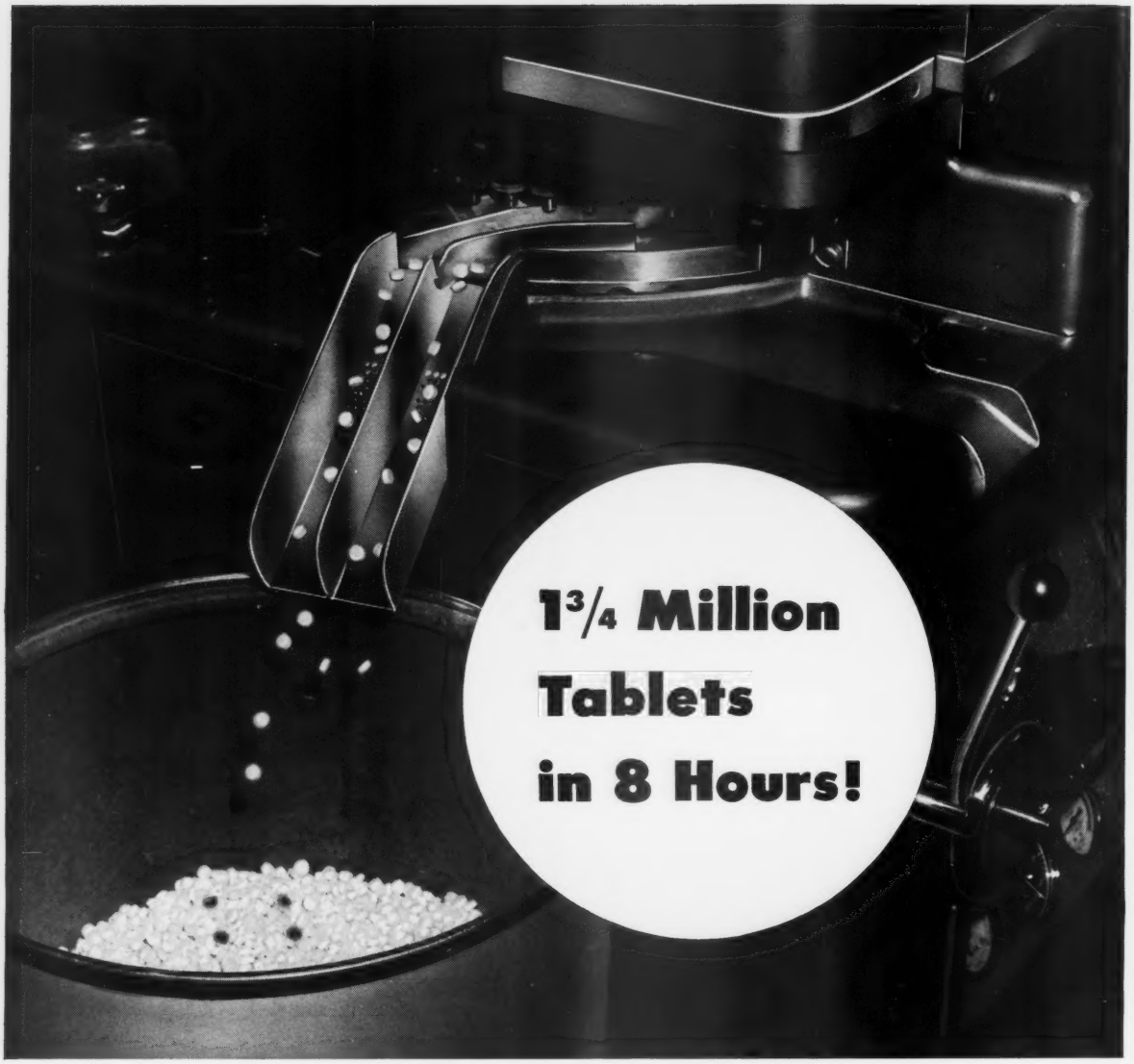


. . . that's the production capacity of the new Stokes Model 551 Rotary Tabletting Press at 3750 tablets per minute.

This is the highest production rate in the industry—achieved with a machine no larger than the well known Stokes Model 540—and without increase in head speed. A new die locking arrangement, called Chord-Loc, permits 51 stations of tooling to be used in a punch circle the same diameter as that of the 540. What's more, you don't have to retool for the 551—it uses the same standard punches and dies as the 540—41 station, and the BB-2—33 and 37 station presses.

You can get complete information on this new four-ton, high-speed machine by calling your nearby Stokes office—or write today.

Tablet Size Specifications
Maximum diameter—$\frac{7}{16}$"
Maximum fill depth—$\frac{11}{16}$"

Pharmaceutical Equipment Division
F. J. STOKES CORPORATION
5500 Tabor Road, Philadelphia 20, Pa.

STOKES

Management Forum

BY FRANCIS CHILSON
INDUSTRIAL CONSULTANT

Management and Men

One of the primary jobs of management is to provide for its own succession. This applies to management at all levels. In family owned corporations the problem takes care of itself, insofar as top management is concerned, because the management mantle is passed on to the owner's heirs, be they boors, boobs or geniuses—the latter being extremely unlikely. But in public corporations management is *morally* bound to provide for its own succession.

I know that a lot of lip service is given this ideal. A lot of articles and books have been written on the subject. But while everybody agrees with this necessity very few managers consistently do anything about it —many of them being afraid to because they might be pushed aside by brighter men. Proof of this is that exceptional men are very rarely employed unless there are immediate jobs open for them. In my entire, long experience I have known only two company presidents who would snatch the opportunity to employ exceptional men even though there was at the beginning nothing for them to do. But *all* company presidents will stock pile raw materials if economic indications that prices are going up or shortages are certain to ensue. But to stockpile brains is not only rarely ever done but to do so is regarded as something of a heresy. Recently I spoke to several company presidents about a job for an exceptional young man, twenty-seven years old, a business administration graduate from one of the best schools, who struck me as so outstanding that I felt compelled to recommend him to several of my clients. The result was the same in every instance. 'We're not taking on anybody right now . . . We're all filled up with non-technical men . . . Business is a bit slow and we're not taking on anybody . . ." The same old silly crap!

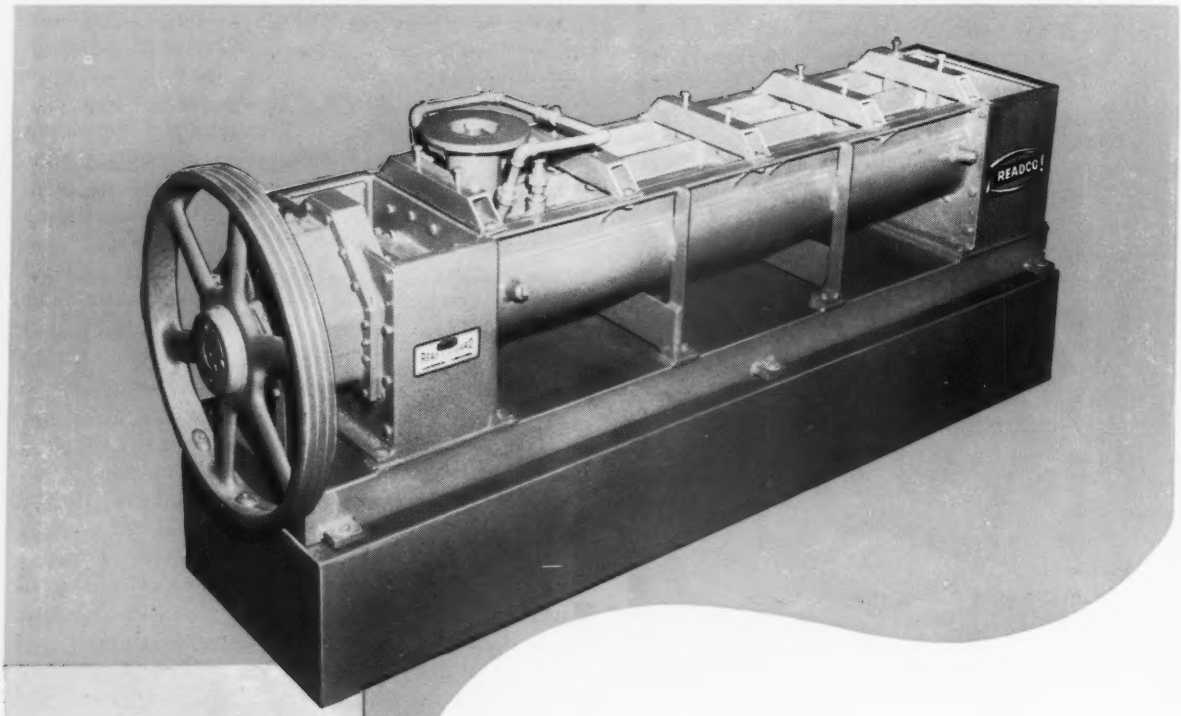
It apparently didn't even occur to a single one of these men that I would not waste a minute of my time on a young man who is not technically trained unless I was certain that he is outstanding.

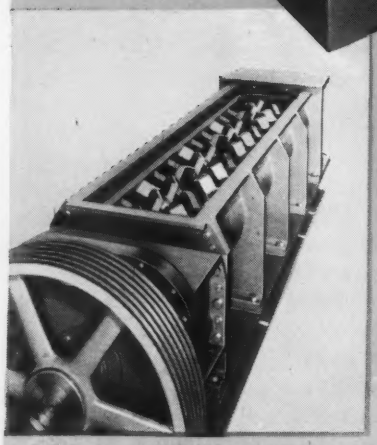
Top management will take a chance on the future and increase marketing appropriations in the hope of increased future sales. Occasionally it will consent to the purchase of new and faster machines, even though similar and workable machines are in current use, in the hope of reduced production costs. But to hire an unusual man when there is no job for him simply isn't done.

But the late, revered John Smith, once president of Pfizer, was an exception. In the depths of the depression he met a young man, who happened to be technically trained, but John Smith had no job for him anywhere in the organization. However, when the young man demonstrated his unusual willingness and faith in himself and offered to take a job as a painter, John Smith hired him. Later he told me it was one of the smartest things he ever did. That young man is still young, still building his company, still demonstarting an immense capacity for leadership. Now he is president of Pfizer. His name is John E. McKeen.

Every company president and every administrator under him should constantly be on the lookout for men of excepptional ability. They need to be on the lookout constantly because exceptional men are not very numerous, hence there is no danger of overloading any organization however large it may be. This job cannot be left to the personnel directors. Most personnel director's are really chief clerks without authority whatsoever to employ anybody unless specifically requested to do so. Many of them wouldn't recognize a man of unusual ability even if they met one.

The large corporations outside the industry have for years combed the graduating classes of the leading universities for technical men of outstanding ability as demonstrated mainly by their grades. DuPont and some other large corporations have since learned that exceptional men can also be found among the non-technical graduates and that technically trained men do not always make good administrators.





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Perfectly Mixed!

Speed production, lower costs...automatically with Readco Continuous Double Arm Mixers

You can step up production and reduce costs of processing dense and viscous materials with this rugged Readco mixer. Built for continuous, automatic operation, it will turn out ½ to 3 cubic feet per minute . . . in a completely homogeneous mix.

Overlapping action of mixing paddles fully disperses ingredients while moving them along to discharge. Temperature controlling jackets for heating and cooling are standard equipment.

For further information on Readco mixing equipment, see Chemical Engineering Catalog pages 1483 to 1490.

Whatever the mixing job: a READCO mixer!

READ STANDARD
York, Pennsylvania

A Division of
Capitol Products Corporation

Every company president and every divisional administrator under him should constantly be aware that they are trustees for their stockholders and also for the next generation. It is their *primary moral obligation* to pass their businesses on in as good a condition or better than they found them. Good, outstanding or even unique products alone will not provide that insurance. All products are subject to obsolescence and competition. Plant, machinery and inventories are of comparatively little value as assets. It takes *men* to translate these assets into products and products into profits.

Able men are the only assets that have permenant value. Able men are the best insurance against the vicissitudes of unpredictable economic and political conditions that confront in ever increasing complexity every business in this country.

Reminiscence

Much has happened during the past quarter century in the drug and cosmetic industries. So many revolutionary things have been done and so many new things introduced, that unless those of us who have passed more than a quarter century in these industries take time out to reminesce a bit, we are apt to forget that much we take for granted now started during our experience in the trade.

For example with all the variety of colored plastic caps available now it is difficult to believe that the first plastic caps introduced in the early twenties were available only in a single color—black. They were Bakelite and they stank of phenol which precluded their use for odor-sensitive cosmetic creams. Bakelite eventually licked the odor. Then came casein plastics with a wealth of colors. But initially they warped and cracked on the containers to which they were applied. Then urea plastics and many others. It was a hell of a job to find a cement that would hold the liners in plastic caps. The Aluminum Company made a valiant effort to invade the market then with aluminum caps that oxidized and smudged badly. Initially colors were not available. It was a far cry from the anodized aluminum caps of today. Long skirted caps became popular for bottles but the capping machines of the twenties would not feed them automatically and it wasn't until the middle thirties that such machines were available.

Cellophane so universal now was a novelty in 1925. When it was first introduced as a wrapping material a good many of the drug houses still wrapped bottles in glassine. At first cellophane was received with skepticism. Its clarity varied. Sometimes it was yellowish. And invariably it cracked upon ageing. But persistent research found the answers. Now we have all sorts of transparent, colored and uncolored, plastic films made from almost everything including wood, rubber and acetylene gas.

Our containers were glass, metal and paper. Now we still have all these in infinite variety but also flexible plastics and gas pressure containers of various types which brought the tin plate manufacturers back into our industries with a bang—with the aerosol containers. Squeeze botles are a far cry from the celluloid shaving cream tube that a Swiss outfit tried to introduce in 1926. It was an appealing idea but the tube smelled of camphor and nobody wanted it.

In 1925 we thought that an automatic bottling line that filled, capped, labelled, cartoned and wrapped at an average speed of fifty containers a minute was a helluva line. There were individual machines that even then ran faster but line operations were slow. By 1935 speed had doubled. By 1945 tripled. By 1955 quadrupled and even quintupled. Nowadays you name the speed and the packaging machinery people will provide the equipment if you are willing to pay the shot. Some indivdual high speed packaging machines now represent an investment larger than a good sized cosmetic plant cost in 1925.

And those lovely smells of the old days. You could smell a cosmetic plant within a block of it. It perfumed the neighborhod. Nobody thought of waste; housekeeping was non existent and all tanks wide open. It was exactly the same with the pharmaceutical industry. You could get a healthy whiff of medicine a quarter of a mile away, mixed occasionally with a trace of sulphides or asofoetida. Those were the happy, carefree days before all these damn chemists came along, when a formula wasn't good unless it had at least twenty or thirty ingredients in it, half of which were incompatible and canceled each other or precipitated out and were thrown away with the filter cake.

The TV spielers nowadays boast about cold remedies that contain three or four ingredients to fight a cold three or four different ways. We used to have cold remedies that contained ingredients to fight a cold twenty-five different ways. Twenty-four of them being worthless. Sometimes twenty-five. Any people who could survive many of the drugs and cosmetics they used to use have nothing to fear from the hydrogen bomb.

Preserving the Unfit

At the National Congress of Parents and Teachers, Dr. Rene J. DuBos of the Rockefeller Institute for Medical Research made the following statement as quoted in the New York Times, May 20, 1958:—

"For the first time in the history of living things, we are allowing the survival of large numbers of biological misfits, many of whom will become a burden for society. Even more significant is the fact that all kinds of hereditary defects that used to be rapidly eliminated by evolutionary selection are now being reproduced in our communities."

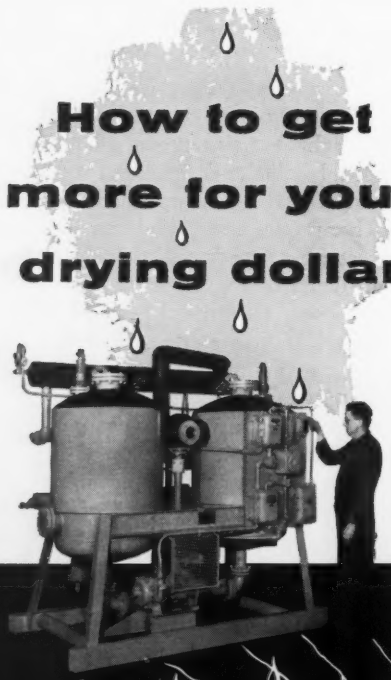
Through the application of medical knowledge in treating diseases, he warned, "we are allowing the accumulation of defective genes in the human stock by providing a type of medical care that permits those suffering from hereditary disease to live longer and to have children."

How to get more for your drying dollar

USERS REPORT that Lectrodryer's reserve capacity —in excess of rated output—helps meet normal production growth over the years with no reduction in drying efficiency. The liberal design and rugged construction of Lectrodryers cut downtime and maintenance costs to rock bottom . . . assure sustained, trouble-free, low-cost drying.

Leading industries look to Lectrodryer for better drying because they have found that our high performance standards result in more efficient, more profitable drying operations.

Our engineers will gladly help you solve your drying problems. Write Pittsburgh Lectrodryer Division, McGraw-Edison Company, 309 32nd Street, Pittsburgh 30, Pennsylvania.



Type BY Lectrodryer for instrument air.

HOW LECTRODRYER WORKS
WET
HEAT
DRYING
air, gas or organic liquid by adsorption
Wet air, gas or organic liquid passes through the desiccant in column A until it has picked up a full charge of moisture. Then this column switches to reactivation, and the material being dried passes through reactivated column B. The cycle is continuous and controlled automatically.
REACTIVATING
Heat drives off entrapped moisture
RESERVE CAPACITY
assures bonus performance . . . less downtime . . . lower maintenance.
DRY
TRAPPED MOISTURE
Leading industries look to
Lectrodryer®
McGRAW EDISON
World's First and Foremost Manufacturer of Commercial and Industrial Adsorbent Driers

"While the preservation of human life is demanded by moral, social and religious considerations, we are now engaged in a process which may result in ultimate dangers." he cautioned.

"This policy may constitute a step toward racial suicide, however noble it may appear in the light of our religious convictions and present-day ethics."

Dr. Du Bos said he did not advocate "a retreat from our human ideals and medical ethics." However, he went on, "we must and will continue to regard all life as secured and worth preserving whatever the cost."

"We also must be aware of the consequences of the new demands and values that we have introduced into the biological arena." he said.

The problems of disease in society "cannot be solved merely by discovering new drugs or investing new surgical techniques," he commented. A reevaluation of social ethics is needed because of the "inevitable limitation of resources" that must be imposed on decisions of the future, he said.

Dr. Du Bos opinion was brought home to me by an incident in my own town. A farmhand in the neighborhood, old, indigent and ignorant was taken to the local hospital two years ago with a heart attack. Something then went wrong with the circulation in his legs. Gangrene set in and his feet were removed. The doctors chopped him up bit by bit until he has no legs left and is now undergoing his fourth operation. If this is medical ethics or Christian ethics or any kind of ethics I am a Chinaman. The poor old man should have been allowed to die two years ago. Right now he is an experimental guinea pig.

Employee Stealing

Recently the Wall Street Journal published a survey dealing with employee stealing particularly in chain and department stores all over the country. The condition is nothing short of appalling. Men and women low, middle and high class personnel are involved. In Seattle the manager of a variety store, which was paying him $135 a week, admitted stealing systematically over a period of many weeks from the charity canisters placed by various organizations in his store! Can anything be more shocking than that? In the trade we have petty stealing especially in the cosmetic industry where all products are useable by the thief or his family or are readily saleable. All this stems back to early school and religious training because we do not lay enough stress upon the sacredness of other people's property as they do, for instance, in England. Over there they have professional thieves of course, but working classes are scrupulously honest. In all my trips to England I have not encountered a case where petty thievery is a problem. In this country I have never heard of a single company conducting an educational campaign against stealing even in cases where the management knows it is going on. If they catch the thieves they fire them without punishment in most cases and prosecution is never attempted unless the thefts have been very substantial. It is up to management to educate their employees about a lot of things they didn't learn at home.

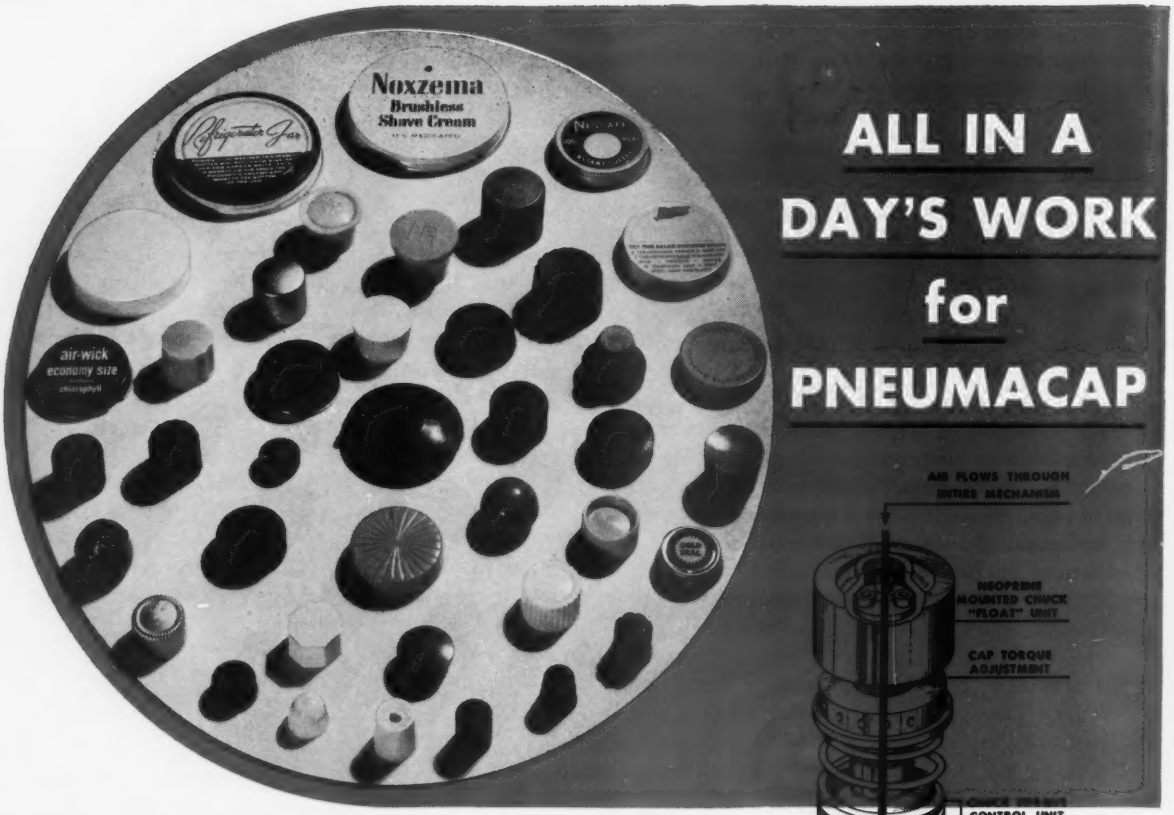
Alcholism

At a recent meeting of the National Council on Alcoholism J. F. Oates Jr., president of the Equitable Life stated his opinion that alcholism costs industry not less than a billion dollars a year. If his statement is true and I think it must be very conservative the pharmaceutical industry is missing a big bet in not doing more research in the field of alcoholism. It is recognized as a disease along with heart disease and cancer but we haven't capitalized on it. Many big companies have programs to rehabilitate alcholic employees. Among them: Con Edison, Eastman Kodak, DuPont, International Harvester—to mention only a few.

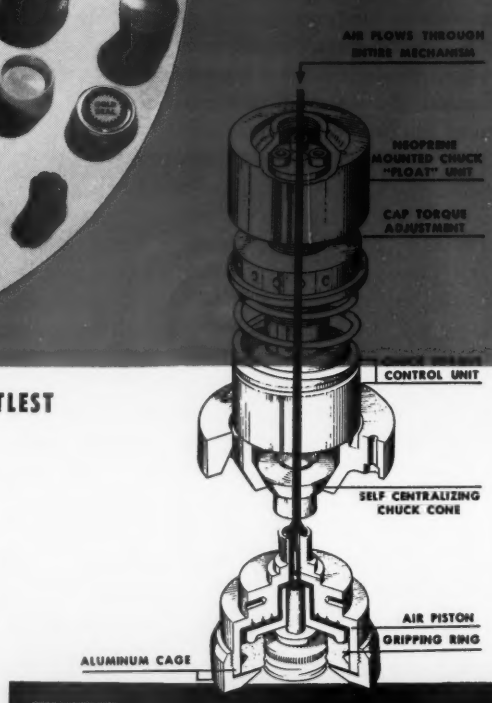
You probably know that alcholism is one of the chief causes of absenteeism and you know what that costs. It is also one of the common causes of tardiness. It is a primary cause of serious accidents and costly mistakes. I could cite hundreds of mistakes that have come under my observation that were directly caused by hangovers. (Some of them my own.) No man with a bad hangover or with a craving for alcohol can keep his mind on his work. He simply cannot think consistently, clearly or rapidly. This is probably truer of the occasional drinker than it is of the habitual drinker. I know several men in the trade who are heavy constant drinkers and who nevertheless are exceptional men. (Most of them in the marketing end of the business.) A heavy drinker as every one knows is not necessarily an alcholic; (Winston Churchill is a good example) and an alcoholic is not necessarily a heavy drinker.

The problem for management is to find out who among its workers and management personnel are affected adversely by alcohol. A good booze party like some conventions I've attended might be a good way to find out. The man who is dangerous is not the guy with a load on who fails to show up; it's the guy who doesn't indicate that he has a bellyfull of booze but who is adversely affected by it, who must be watched. Some research on pharmaceutical antidotes has been done and Dr. Henry Koch Jr. of the Southwestern Research Institute of Tucson, Arizon, has had some remarkable results in the treatment of alcholism with triiodothyronine, known as T3. This may be an answer.

It is inspiring to realize that some managements are attacking the problem intelligently and are trying to salvage their own people. In the old days a drunk was fired unless he was the boss's son or the boss himself. Some bosses can hold an awful lot of liquor. But it's a difficult thing to conduct an educational program when everybody in the organization knows that the Old Man gets as full as a boot regularly.



ALL IN A DAY'S WORK for PNEUMACAP



AMAZING ADAPTABILITY COUPLED WITH THE GENTLEST FEED AND TURN-ON ACTION KNOWN

Right from the time the caps are delivered to the hopper of the Sterling Cap Feeder on the PNEUMACAP, to the moment they're turned onto the container, they're handled with kid gloves. There's no churning or grinding in the feeding operation. Caps "dribble" easily into position, on call from the machine. No jamming to cause scratching or breakage.

Then the amazing air chuck takes over. Air pressure firmly squeezes the neoprene doughnut around the cap. Exactly conforming to any turn-on closure – metal, knurled, smooth, molded – it holds the cap in its no-scratch, no-slip grip. Full floating action allows chuck and cap to "find" container top. Choice of four chuck speeds to match caps from partial turn-on lug type to multi-turn long continuous thread closures. Machine is available in two, four, six and eight head models.

PNEUMATIC SCALE CORP., LTD., 70 Newport Ave., Quincy 71, Mass. *Also: New York; Chicago; Dallas; San Francisco; Los Angeles; Seattle; Leeds, England. Canadian Division: Delamere & Williams Company, Ltd., Toronto.*

★ PNEUMATIC

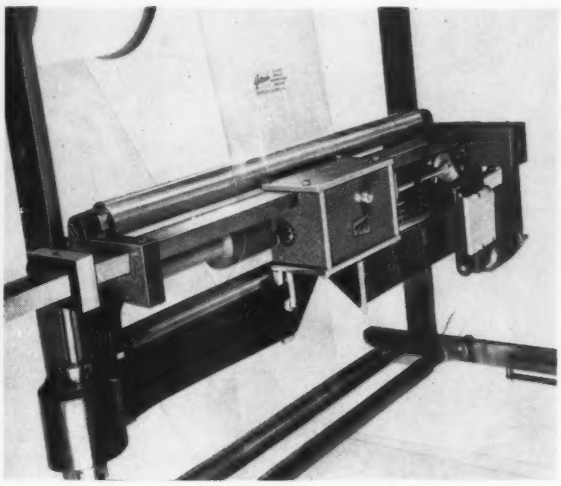
Packaging and Bottling Equipment

Once when I was visiting a client's plant the president, who liked his liquor, called me on the phone and asked me to come to his office immediately. I did so promptly and found he was not at his desk. So I stepped into his secretary's office and said, "Where the hell is the Boss; he's not at his desk." She said, "Have you looked under it?"

New Imprinting Attachment For Continuous-Feed Wrappers

A new model roll-leaf imprinting attachment that operates on continuous-feed wrapping and bag-making machines has been introduced by Adolph Gottscho, Inc.

The new model P-11 Wrap-A-Printa attachment is a compact unit that operates like an automatic type-



writer, making crisp rub-proof impressions of code dates or other legends through a ribbon of inexpensive leaf material. This is said to eliminate any ink-drying problems on hard-to-print stocks, such as wax paper, polyethylene, cellophane and foil. According to the manufacturer, 1000 code-date impressions can be obtained with as little as 5 cents worth of leaf, which is available in various colors.

Conical-Shaped Rotating Vacuum Dryers

A new series of conical-shaped rotating vacuum dryers, Model 159, in a range of six sizes: 3, 10, 25, 75, 100 and 150 cu. ft., has been added to the line of vacuum drying equipment offered by the Vacuum Equipment Division of F. J. Stokes Corporation, Philadelphia.

The Model 159 series incorporates many of the proven design features of other Stokes dryers, which have met industry's requirements for efficient vacuum drying techniques for many years.

The conical shape offers distinct advantages over conventional cylindrical-shaped rotating dryers in charging and discharging the material being dried, and also provides a better tumbling action. This means a drying rate at least as good as, and in some cases better than, that obtainable with the cylindrical design.

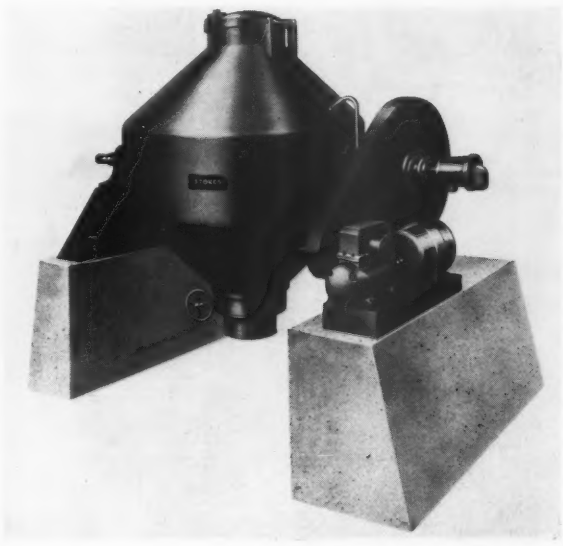
The new conical dryers have drums of double-walled construction for steam or hot water heating. Interior surfaces that come in contact with corrosive product or product vapors are fabricated of Type 304 or 316 stainless steel. The drum is designed for operation at full vacuum and at atmospheric pressure on the interior; the jacket for operation at a steam working pressure of 50 p.s.i.g., or for hot water.

The charging inlet has a full-opening hinged cover suitably gasketed and equipped with a quick-opening clamp-type hold-down mechanism. The discharge opening is provided with a self-wiping vacuum tight valve, which is worm-gear operated and fitted with neoprene seals.

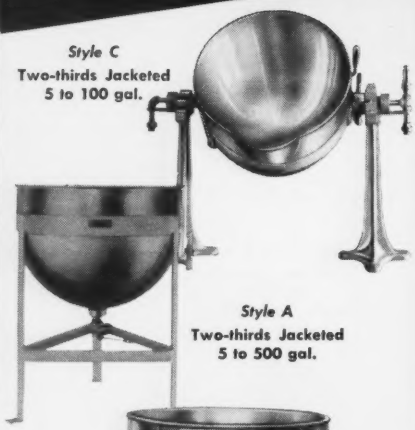
Several dust collecting systems are available, depending on the characteristics of the material being dried. A full-sized flanged connection is provided for the vacuum line to remove the moisture and other vapors. The diameter of the line will vary with the nature of the material to be dried, and with the cubic contents of the dryer. The inlet to the vacuum line within the dryer is capped with a filter, to protect the vacuum pumps and vacuum line from dust carry-over. For material that dusts very heavily, the filter is mounted externally for greater convenience in cleaning. The vacuum line itself is stationary and enters the rotating journal of the dryer through a chevron-type vacuum seal.

The complete dryer assembly, with both of the openings closed, is tested for vacuum tightness with a mass spectrometer before shipment.

The dryer is rotated at a fixed speed of 6 rpm by means of an electric motor and a suitable speed-reducer which in turn drives the dryer through a chain and sprocket assembly. The chain is protected by an oil-tight chain casing.

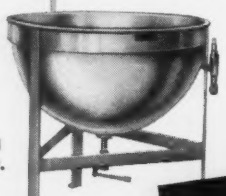


COOKING KETTLES

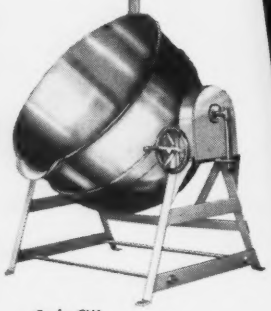


Style C
Two-thirds Jacketed
5 to 100 gal.

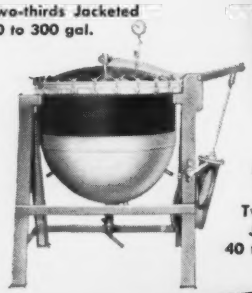
Style A
Two-thirds Jacketed
5 to 500 gal.



Style B
Full Jacketed
10 to 300 gal.



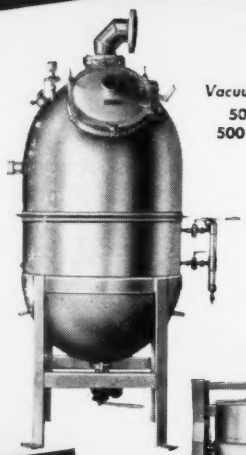
Style CW
Two-thirds Jacketed
80 to 300 gal.



Pressure Kettle
Two-thirds Jacketed
40 to 200 gal.

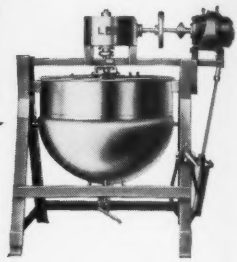
MIXING AND BLENDING UNITS

CW3T
Center-line Scraper Agitator Kettle
80 to 300 gal.



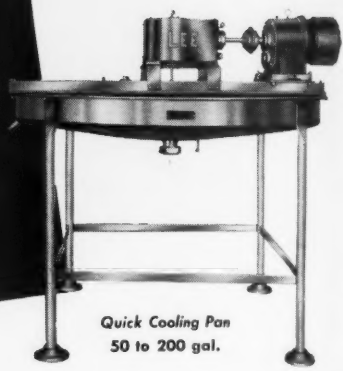
Vacuum Pan
50 to 500 gal.

D3T
Center-line Scraper Agitator Kettle
25 to 300 gal.



these LEE Units

WILL REDUCE YOUR PROCESSING COSTS!

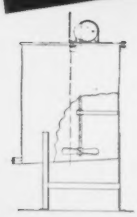


Quick Cooling Pan
50 to 200 gal.

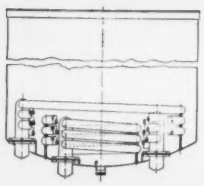
Individually designed for a specific processing operation and available in a wide range of sizes to fit your exacting requirements, Lee corrosion-resistant equipment is built to give you long years of peak performance with minimum maintenance.

Descriptive bulletins are available for any or all of the above units. Write for them today and discover how Lee can help reduce *your* processing costs.

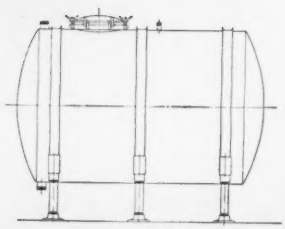
MIXING, COOKING & STORAGE TANKS



Mixing Tank
25 to 500 gal.



Pulp Tank
500 to 2,000 gal.

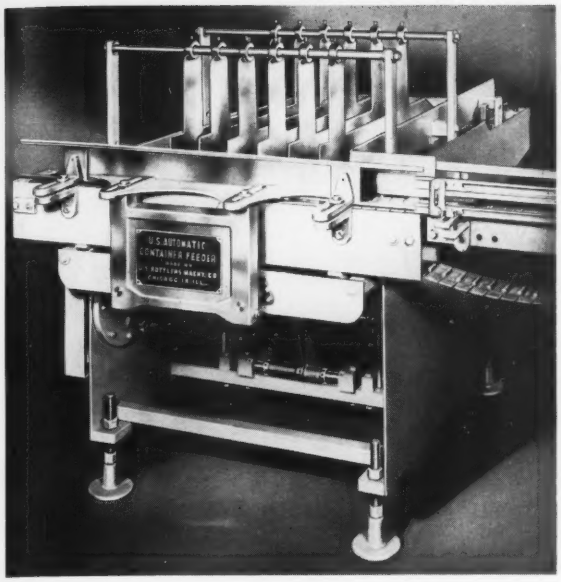


Storage Tank
100 to 5,000 gal.

LEE METAL PRODUCTS CO., INC.

408 PINE STREET, PHILIPSBURG, PA.

ALL LEE KETTLES ARE MADE TO A.S.M.E. CODE



Container Feeder by U.S. Bottlers

The new U.S. Container Feeder handles rounds, squares, panels, ovals in glass, cans or jars. Quick adjustment is made for containers from about ¾ to 4 and ½ in. in thickness, as well as for larger containers on special order.

The machine feeds containers as quickly as the packaging line can absorb them. As each row of containers advances intermittently on a moving mesh belt, a retractable discharge guide releases each row to the conveyor as soon as the preceding row has cleared. Variable speed ratio of 2 and ½ to 1 is regulated by the turn of a crank. To accommodate the number of containers per row as packed, 6 adjustable separator plates are supplied with a standard machine. Additional separator plates are available for more rows.

The driving mechanism is of the same general design as that of other U.S. Bottlers packaging equipment. The machine is built on a rigid steel frame with steel-enclosed sides. Carton lint drops through the wire-mesh belt into a dust collecting pan, and, due to precision mechanism with a minimum of wearing parts, the machine requires a minimum of servicing.

High Speed Overprinting Possible With New Markem Machine

Die-cut pressure sensitive paper, gummed paper and other types of labels in roll form that are partially preprinted may be overprinted with extremely accurate registration, or marked completely from blank stock, with a Markem Model 126AF machine. An automatic feed checker assures perfect alignment of label stock, such as that used for bakery labels, clothing size tickets, woven labels, small button or hang tags, etc.

The stock is fed from a roll, printed or imprinted and then either re-rolled, perforated and re-rolled, or cut and stacked. Operating speeds from 70-100 labels per minute may be attained depending on label material and size. The Model 126AF machine will make imprints up to 2″ x 3″ using rubber plates or typeholders such as Markem masterplates with insertable type. Short runs and frequent variable changes are practical on the 126AF, since type can be changed in a matter of seconds. Markem specialty inks for all surfaces and materials are available in standard or special colors, to meet a variety of durability, drying or special requirements.

The Model 126AF machine may also be equipped with an automatic counter which stops the machine when a preset number of labels has been printed, or with a reset counter to indicate the number of labels printed. Specifications of the bench mounted Model 126AF include ¼ hp motor drive; overall dimensions, 45″ x 17″ x 33″ high. Further details are available on request from Markem Machine Co., Keene 64, N.H.

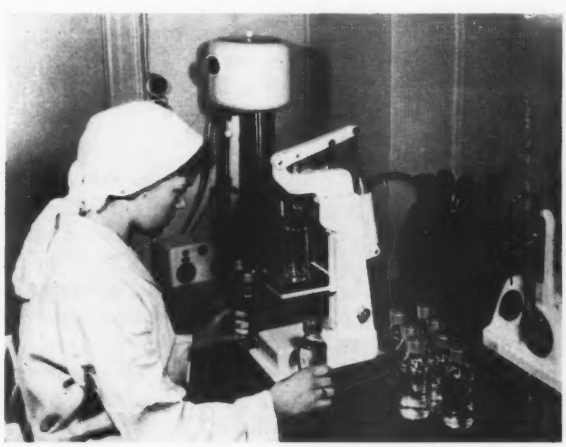
Improved Capping Machine

A new, semi-automatic Capsolut capping machine, claimed to be 100 per cent more productive than previous hand-operated machines, has been announced by Arenco Machine Company of New York.

Operated by compressed air, the cap seating and sealing mechanism is controlled by a foot treadle, permitting the operator to use both hands for loading. Two easily adjusted valves determine and maintain the pressure required for perfect sealing, which corresponds to the strength and resistance of the capping material. This ranges from 35 to 42 lbs. per sq. in. for 20 mm. caps, up to between 71 and 100 lbs. per sq. in. for larger and heavier caps.

The machine, which is neat and compact, handles vials, aerosols and other containers in heights from 40 to 240 mm., and diameters from 8 to 100 mm.

Said to be ideal in design for the capping needs of small as well as large operations, the Capsolut is equipped with necessary safety devices, moreover, it can be operated by unskilled personnel.



Industry's Books . . .

Topics In Microbial Chemistry, *by F. M. Strong, Department of Biochemistry, University of Wisconsin, 166 pp., John Wiley & Sons, Inc., New York, (1958), cloth,* **$5.**

This volume presents an account of antimycin, kinetin, and coenzyme A, covering their basic chemistry, preparation, and properties. It is based on the first series of E. R. Squibb Lectures on Chemistry of Microbial Products at the Institute of Microbiology, Rutgers University. Dr. Strong furnishes the only published survey of antimycin, now a standard tool of biochemical enzymologists. Coenzyme A purification and chemistry are more critically reviewed than in any other book. Of special interest to researchers is his treatment of kinetin and the kinins, a newly discovered group of plant hormones that may develop in importance as much as the auzins. These substances have in common the fact that they are obtainable from microorganisms and are physiologically active at very great dilutions.

Drugs, Their Nature, Action And Use, *by Harry Beckman, M.D., Director, Departments of Pharmacology, Marquette University Schools of Medicine and Dentistry, 728 pp., W. B. Saunders Co., Phila., (1958), cloth,* **$15.**

This is a textbook for the undergraduate medical student. His need is for a special type of book with which to supplement his studies in the laboratory and lecture and conference rooms. It is written in three distinct portions. In Section I the attempt is made briefly to orient pharmacology among the other preclinical disciplines. In Section II there is presented a description of the broad background of the science and an exposition of the bases from which advances are made. Section III, which comprises the major part of the text, offers combined discussions of the actions and actual uses of drugs in an arrangement designed for direct serviceability from the pharmacotherapeutic standpoint. The biobliographies serve as a guide for excursions into the literature.

The Extra Pharmacopoeia Martindale, Volume I—*twenty-fourth Edition, 1958, Published by direction of the Council of The Pharmaceutical Society of Great Britain, by The Pharmaceutical Press, London, 1695 pp., bound,* **£3.52 Postage 3s.**

Accepted throughout the world for 75 years as an invaluable source of information on medicinal and pharmaceutical substances this entirely new 24th edition of Volume I has been completely re-written and revised and is up to date in respect of the wide field of therapeutics which it covers. It forms the most complete guide to "ethical" proprietaries and to formulas from many sources including those in foreign pharmacopoeias. There are several sections on antibiotics, biological products, and drugs that are rarely used. Details are provided on the toxicity of chemicals and drugs, on reports of cases of poisoning, and on treatment of overdosage. The book is much larger and has more pages than any previous edition.

Ocular Allergy, *by Frederick H. Theodore, M.D., and Abraham Schlossman, M.D., 420 pp., Illus., The Williams & Wilkins Co., Baltimore, (1958), cloth,* **$12.00.**

This book correlates and classifies the clinical manifestations of ocular allergy in accordance with the various allergic mechanisms involved. Consideration of the subject has been tempered and disciplined by the authors's studies and experience in the related fields of ocular microbiology, external diseases and therapeutics. Utilizing accepted allergic principles, they have been able to interpret ocular hypersensitivities, with only few exceptions, within the basic categories of anaphylactic, atopic, microbial, and contact reactions. With this work the clinician should be better equipped to recognize and evaluate the many forms which ocular allergies assume, and to resolve many otherwise troublesome therapeutic problems arising from the fact that different allergic responses make necessary different types of treatment.

New And Nonofficial Drugs 1958, *645 pp., J. B. Lippincott Co., Phila., cloth,* **$3.35.**

This contains descriptions of therapeutic, prophylactic and Diagnostic Agents evaluated by the Council on Drugs (Formerly, Council on Pharmacy and Chemistry) of the American Medical Association. It is an annual publication issued under the direction and supervision of the council. Descriptions of drugs are presented under nonproprietary names in the form of monographs designed to provide the following information: chemical or biologic identity, including pertinent properties; actions and uses, including associated side effects, toxicity, and percautions; and dosage.

Oral Communication of Technical Information, *by Robert S. Casey, W. A. Sheaffer Pen Co., 199 pp., Reinhold Book Div., New York, (1958), cloth,* **$4.50.**

Methods of effective speaking for almost all situations are assembled here for technical men. Beginning with the bridges and barriers to effective communication, the book then takes up the actual problems involved and how they are solved. It covers organization of material, composition, delivery of formal and impromptu speeches, and the use of mechanical aids such as recordings and slides. How to preside at meetings, talk science to laymen, give technical legal testimony, and converse socially are covered in helpful detail. Emphasis is on the special needs of technical subject matter, but the techniques of organization and delivery apply generally.

An Introduction To Pharmacology And Therapeutics, *by J. A. Gunn, C.B.E., M.D., with the assistance of J. D. P. Graham, M.D., Ninth Ed., 327 pp., Oxford University Press, London, (1958), cloth,* **$4.25.**

Professor Gunn and Dr. Graham have between them rewritten the greater part of the text for this new edition and they have given accounts of all new drugs that, in their opinion, merit inclusion. Some increase in the length of the text has been inevitable but they have not departed from the original aim of the book—a short but comprehensive survey for medical students, achieved by selection and arrangement.

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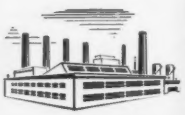
MANUFACTURING DEPARTMENT 	High and rapid solubility.	Compatible in multivitamin formulae.	Economical, less time and labor in compounding.	No solubilizer needed.	Make clear solutions of 30 mg. or higher per ml. of water.	No special techniques required. Relieve technical department problems.
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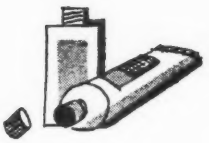


Advancing Therapy

Phenolic Compounds for Rheumatic Fever

Compounds related to the monophenol salicylic acid, i. e., the diphenols gentisic acid, protocatechuic acid, 2,3-dihydroxy benzoic (pyrocatechuic) acid, beta resorcylic acid, and gamma resorcylic acid, and the triphenols phloroglucinol carboxylic acid and 2,3,6-trihydroxy benzoic acid, were tested by N. E. Clarke, C. N. Clarke and R. E. Mosher (*Am. J. Med. Sci.* 237:7, 1958) in patients with rheumatic fever and rheumatoid arthritis. Increased antirheumatic potency was observed in phenolic compounds with double che late rings, and superior antirheumatqualities were associated with a second or third hydroxyl group in the 3 position on the benzene ring. The compounds that had double chelate rings or a single chelate ring and hydroxyl group in the 3 position did not generate usual urinary changes associated with detoxication. The phenolic compounds produced some changes associated with antirheumatic adrenal hormones but differed by producing relative increases in circulating lymphocyte cells and decreasing the urinary excretion of 17-ketosteroids.

The high antirheumatic potency of double chelating phenols supports the importance of antirheumatic metabolites in salicylic acid therapy. The compound 2,3,6-trihydroxy benzoic acid had lower toxicity and acted more promptly to suppress manifestations of rheumatic fever and lower elevated blood sedimentation rates than did all other phenolic compounds. Like other double chelating phenols in this series, it usually decreased urinary excretion of sulfur and glucuronic acid conjugates except in patients who had malignant or submalignant rheumatic fever. These metabolic findings suggest normalizing or saving action on special connective tissue components. The compound 2,3,6-trihydroxy benzoic acid also produced significant and consistent reduction in the urinary excretion of 17-ketosteroids, which lends support to its having a saving action in rheumatic fever. These observations permit the belief that triphenols and especially 2,3,6-trihydroxy benzoic acid, when administered early in a first attack of rheumatic fever, bring unusually rapid recovery without residual signs of heart damage.

Press Agent's Triumph

The New York "World Telegram and Sun" was taken for a fine ride by a press agent in a story reported recently. According to the story, the only amateur radio operator in Bilbao, Spain sent out a distress call for Squibb's Tolserol. The call was picked up by a "ham" in Grangano, Italy who relayed it to South America from where it went to New Zealand, then California and finally was picked up in New Jersey. "The Squibb Co. was contacted, the precious drug obtained. It left Idlewild Airport on a special mercy plane of Iberia Airlines. It is expected to reach Bilbao this evening—in time to save a life". Mephenesin, toloxypropanediol, the generic and chemical names for Tolserol, is seldom if ever required in life-saving situations and certainly available without trouble in practically any drug store in any civilized city in the world. Who planted this one?

Drug Side Reactions and Anesthesia

This paper by J. W. Dundee (*Brit. Med. J.* 1958, 1433) draws attention to the increasing use in medicine over the past few years of drugs which influence the response of patients to anesthesia. This side-action cannot usually be predicted by pharmacologists, and often it was detected only by chance when the preparation in question had been in clinical use for several years. In all the instances reported the effect was to engender in patients an increase in toxicity of one or other of the effects of general anesthetics.

Therapeutic agents whose main effect is to decrease vascular tone, such as the ganglion-blocking drugs or chlorpromazine, if given before anesthesia, increase the hypotensive action of the narcotics, and severe and even fatal collapse may follow what are considered to be normal doses of anesthetic drugs. This applies particularly to the intravenous barbiturate anesthesia, where it is difficult, even in normal subjects, to predict the degree of hypotension that will follow injection and to adjust the dose so as to minimize this action. Care must also be taken in anesthetizing patients who are receiving other hypotensive agents such as the rauwolfia or veratrum alkaloids or mecamylamine.

Clinical and experimental evidenc shows that the phenothiazine derivatives prolong the narcotic action of anesthetics. This also seems to apply to the non-phenothiazine preparations which are used for the control of tremor in Parkinsonism, and possibly may be a side-effect of all the tranquilizers.

A dangerous degree of respiratory depression can result from the combination of analgesic drugs and the intravenous barbiturates. A similar result can occur when cyclopropane is administered to patients who have had deep x-ray therapy to the head and neck.

Induced adrenocortical insufficiency, following the prolonged use of cortisone, its analogues, and corticotrophin, makes patients sensitive to

the stress of surgery and anesthesia. Prolonged severe hypotension, respiratory depression, and delayed recovery may follow surgical operations in such patients. Increasing use of the steroids is focusing attention on this hazard, and especially so in minor cases, where one does not normally associate any risk with anesthesia. It must also be stressed that steroid-induced primary pituitary failure may persist for several months after stopping the drugs.

The hazards of inducing anesthesia in patients with a full stomach are now widely appreciated, and for this reason the pre-operative preparation of diabetic subjects with oral glucose is deprecated. Other problems which anesthetists may encounter are the incompatibility of pitocin with light cyclopropane anaesthesia and the possibility of citrate intoxication as a differential diagnosis for cardiovascular collapse after massive transfusion of stored blood.

In very few of the cases reported did the anesthetist know of the use of various drugs before operation, or associate hypotension or prolonged unconsciousness with any form of routine medical treatment. It is hoped that this publication will focus the attention on the fact that during anesthesia unexpected adverse effects may be produced by drugs which do not appear to have any side-effects in the conscious subject. It is to be expected that many additions to the list of drugs discussed above will be noted in the future.

New Penicillin Salt

A new salt of penicillin of prolonged action, whose chemical name is 2,5-diphenylpiperazine bis-benzylpenicillin G, was studied by G. Orestano (*Minerva Med.* 48:4107, 1957) with reference to the duration of the concentration in blood and its clinical effects in 2 groups of persons. A single, intramuscularly administered dose of 2,5-diphenylpiperazine bis-benzylpenicillin G amounting to 500,000 units was given to 14 persons; the same amount of procaine penicillin G was administered to 8 persons. Neither group had ever before received penicillin therapy. Serum specimens were obtained 2, 3, 12, 24, 32, 48, 72, and 96 hours after the administration of these 2 drugs. The 2,5-diphenylpiperazine bis-benzylpenicillin G proved to be a drug of prolonged action. This has been demonstrated by its concentration in blood of over 0.05 unit per cubic centimeter for a period of 48 or more hours after the administration of a single dose; the level persisted for 72 hours in 4 patients and for 96 hours in 2. A concentration of procaine penicillin G in aqueous solution of over 0.05 unit per cubic centimeter never persisted 48 hours after its administration; this level was maintained for only 32 hours in 4 patients and for 24 hours in 4.

Clinical effects of 2,5-diphenylpiperazine bis-benzylpenicillin G were studied in 45 patients who had an infectious disease or in whom the therapeutic effect of penicillin was already known. They received the drug in a single intramuscular daily dose of 500,000 units for a period of between 2 and 16 days. The patients tolerated the drug well. Two patients, in whom previous administration of procaine penicillin G produced unfavorable side-effects, had no complaint about 2,5-diphenylpiperazine bis-benzylpenicillin G. This new salt of non-procaine penicillin has thus proved to have a more extended action and to be better tolerated by the patients than procaine penicillin G.

New Analgesic

Animal experiments carried out by Janssen and co-workers showed that the analgesic effect and the therapeutic range of 2,2-diphenyl-3-methyl - 4 - morpholino - butyryl - pyrrolidine in dextrose (R 875) make it the most active of the analgesic drugs know today that have a low toxicity. G. Boudin and J. Barbizet (*Presse Med.* 66:131, 1958) tested the effect of R 875 on the threshold of perception of pain in normal persons. After the administration of 10 mg. of R 875, the sensitivity to such stimuli as pinching of the skin, of the nails, and of the testes, which as a rule are painful, was reduced, with some of the persons tested having less pain and some having no pain whatsoever.

Clinical experience with more than 100 patients with various painful conditions revealed the favorable action of the drug on meningeal pain and pain resulting from cancer. But the most remarkable effect of R 875 was observed in patients with pain which up to now proved to be refractory to any medical treatment.

R 875 may be administered orally or subcutaneously; the intravenous route of administration is contraindicated because of the risk of respiratory accidents. Certain undesirable side-effects of the drug, such as malaise, nausea, vomiting, and occasionally drowsiness, require care in administering it; rest in bed is advisable, at least for the initial phase of the treatment.

Drug for Hypertension

A recently introduced ganglion-blocking drug, pemipdine[1,2,2,6,6]-pentamethyl piperidine, is effective in the therapy of hypertension in man according to M. Harrington, P. Kincaid-Smith and M. D. Milne (*The Lancet* II: 6, 1958)

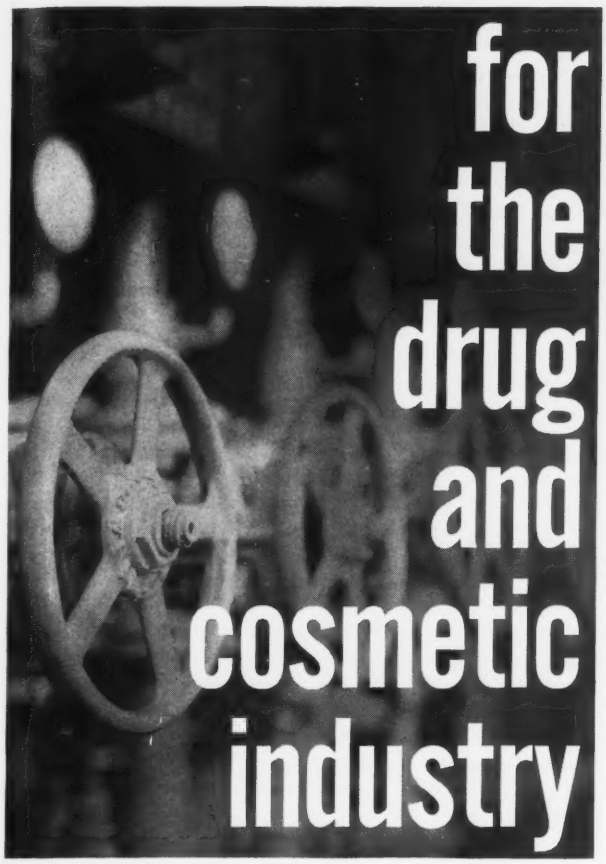
It has many points of similarity to mecamylamine. Both are freely absorbed from the gut, as a result of which a constant therapeutic effect from day to day can be obtained with oral administration. Both are excreted more rapidly in acid than alkaline urine, are concentrated in tissue containing a high proportion of cell nuclei, and easily cross the blood-brain barrier.

Several differences in detail make pempidine a potentially more useful drug than mecamylamine. The excretion of pempidine is more rapid, chiefly because of a lower tissue affinity for the drug. Excretion of pempidine is less affected by variation in acid-base balance than that of mecamylamine. The difference between an effective and a toxic concentration is probably greater in the case of pempidine.

A steady hypotensive effect can be maintained throughout the day when pempidine is given orally at five-hourly intervals. The dosage of pempidine can be quickly increased, owing to the rapid elimination of the drug.

Thin-Down

This, by Revlon, is a combination of phenylpropanolamine hydrochloride (mispelled on the labelling as phenylproponolamine) with vitamins and minerals, providing in each three tablets, 75 mg. of the appetite-depressant and minimum daily adult requirement of vitamins A, B_1, B_2, C, D and niacinamide and of iron and iodine among others. The preparation is available in cartoned bottle containing 90 tablets along with a purse tablet container.



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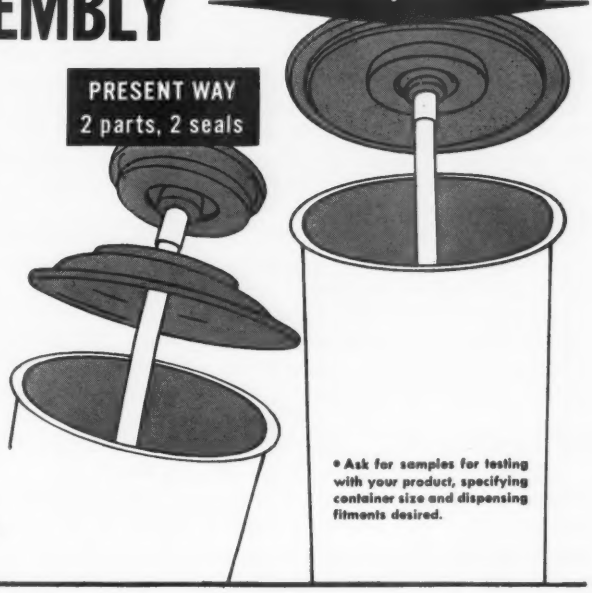

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Black Pepper Oil

Malabar black pepper, cured by sun-drying and containing 5.9 per cent fixed oils and 3.2 per cent volatile oils, was ground in a mill and the slurry distilled with steam. The distillate was extracted with ether and the ether solution washed to remove basic and acidic constituents.

The basic fraction of the oil was found to contain piperidine, estimated to constitute 0.1 per cent of the total oil.

The higher boiling constituents, consisting of oxygenated compounds and sesquiterpenes, were separated into a hydrocarbon and an oxygenated fraction.

The higher boiling hydrocarbon portion was redistilled at 135 to 145° C./24 mm. β-Caryophyllene, which formed 19 per cent of the oil, was present among the sesquiterpenes and there was a blue residue of azulene.

A crystalline compound, present in the eluates, was found to be epoxydihydrocaryophyllene, which has also been found in small amounts in steam-distilled clove oil.

The other oxygenated compounds of the pepper oil, besides caryophyllene oxide, were dihydrocarveol (2 per cent of the original oil), piperonal (0.5 per cent), and cryptone (0.1 per cent) together with traces of mono- and sesquiterpene alcohols. It is considered that these oxygenated compounds are responsible for the characteristic odor of the oil, and the result of this work might be of use if it was ever necessary to formulate an acceptable synthetic pepper.

Flavor

Flavor is essentially a mixture of sensations of our nervous system, perceived by our senses of smell, taste, and touch.

The largest contributing factor, in most cases, is odor. This can be illustrated by the fact that with the nasal passages blocked and the eyes blindfolded, it is almost impossible to distinguish between a raw onion and a raw potato.

Odor is perceived in the nose by means of receptor centers which are extremely sensitive. Experiments have shown that the odor of certain compounds can be perceived in concentrations as low as one part in in forty or fifty million.

There are a number of theories on odor perception. It is believed to be an infra-red or chemical phenomenon by some and an electrical phenomenon by others. No theory has been proved conclusively because the process is extremely complex, and measurements are difficult to obtain.

The mechanism of odor perception is really amazing because the number of odors that can be differentiated is practically unlimited, and past impressions are wiped out almost immediately. A good perfumer can distinguish and remember several thousand odors while the average person knows a few hundred, based on past experience.

The physiology of taste has been much better established. There are only four basic tastes: sweet, sour, bitter, and salty. The tongue has definite, specific receptors for each taste, arranged in a pattern which has been well-established experimentally. However, the taste picture is complicated by the fact that different people respond in a different manner to some taste stimuli. For instance, sodium benzoate, a food preservative, is tasteless to most people, but to others it is sour, sweet, bitter, or salty.

Psychologically, our flavor habits are governed to a large extent by environment and heredity. Different population groups have different likes and dislikes. Flavor habits are also shaped by past experience, which is essentially an environmental factor, and some people like to think of our flavor habits as conditioned reflexes. Hereditary traits, such as an innate high or low sensitivity to specific odors and tastes, also contribute to flavor acceptance patterns.

Of course, there are many other factors that influence the response to flavor stimuli and help govern flavor preference. Climate, age, frame of mind, thought association, stress, and physical health are just a few.

Flavor is also affected by texture, which is perceived by our sense of touch. Lettuce, for example, is practically tasteless but has a very crisp texture. Other minor sensations which are considered to be part of flavor include astringency, such as a lemon which makes the mouth pucker; heat, such as we feel when we bite on a pepper corn; and coolness as exemplified by the effect of menthol.

It has also been found that flavor perception is influenced by the sense of sight, as evidenced by the fact that most fruit-flavored gelatin desserts will have an orange flavor when eaten under a strong orange light.

—K. S. Konigsbacher, Evans Research & Development

Pentione

From its basic synthesis, Hoffmann-La Roche Inc. has developed a completely new aromatic material, now being produced on a commercial scale, to which the name "Pentione" has been given.

The original compound, Pentione AR-1000, is a new ketone chemically related to the ionones and it is being offered commercially in a number of different forms. All forms have a

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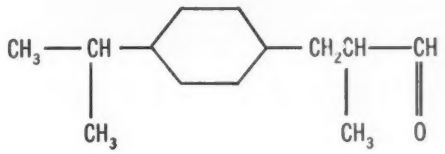

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SPECIFIC GRAVITY $(\frac{25}{25})$**:**	0.950
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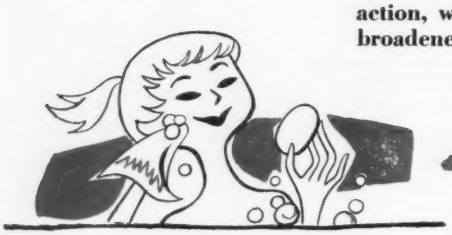

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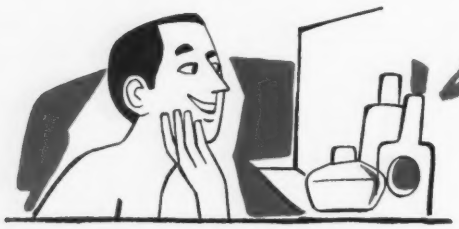

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good labdanum and woody or earthy type of odor and blend well with most essential oils and aromatics. Their low price and high order of stability permit their use in soaps and detergents.

Pentione Extra (AR-1001) has been chemically treated to enhance the basic character of the odor. Pentione "D" (AR-1002) and Pentione "R" (AR-1003) have been partially hydrogenated by different routes. Pentiol (AR-1004) has been fully hydrogenated and converted into the corresponding saturated secondary alcohol.

Pentione (AR-1000) has a slightly citrus-like odor, with a good woody, labdanum, amber-like background that blends well with most types of odors, especially those requiring a citrus-type top-note.

Because of the basic character of its odor, this Pentione performs excellently in fougeres, ambers, chypres, leathers and other types of compositions where the character of the amber note is desirable. As much as 30 percent Pentione (AR-1000) can be used, without fear of its dominating the compound. The earthy and woody tones also aid in achieving the patchouli - vetivert effect, which is usually associated with labdanum in such compositions. With its citrus-like top-note, Pentione (AR-1000) has a lifting effect, which makes it possible to reduce the amount of citrus oils normally used in fougere and amber for this purpose. The material blends well with ionones and contributes to their fullness, while adding a light, fresh top-note. Small amounts are useful in modified eau-de-colognes, as well as in neroli and orange-blossom compositions.

Pentione Extra possesses the same type of odor as Pentione, except for the fact that the citrus top-note has been almost eliminated and the amber character is thereby increased.

Basically, Pentione 'D' has the same type of odor as Pentione Extra, but the partial hydrogenation has increased the labdanum and amber character. In general, the unhydrogenated Pentiones are brighter, whereas the hydrogenated forms have lost some of the brightness but have gained in depth and warmth.

The odor of Pentione 'R' is slightly different from that of the other Pentiones, since it is a definite woody type with a rosy, wine-like or fruity top-note. This character renders it suitable for many floral compositions, as well as for the types suggested for the other Pentiones. It functions excellently as a base for powder perfumes and is particularly useful for creams, since it does not discolor as many natural labdanum materials do.

While it has a definitely woody character with a warm, amber tone, the odor of Pentiol has a definite floral quality. It recalls the odor of cananga and therefore makes a very suitable base for Ylang Ylang. Up to 50 percent Pentiol can be used for this purpose. The particularly tenacious and woody odor suggests its use in perfumes where woody notes of the vetivert type are used. In geranium compositions, for instance, it helps the woodiness of the geranium odor and can be used in such compounds up to 20 percent. Pentiol is very lasting and has good fixative properties.

Diet for Phenylketonuria

A new, complete formula product Lofenalac for the dietary management of phenylketonuria, a hereditary disease which causes mental retardation in children, has been developed in the Mead Johnson & Company research laboratories.

Phenylketonuria is a little known disease resulting from a congenital inability to metabolize phenylalanine properly.

Clinical research to date indicates a low phenylalanine diet will help prevent the mental deficiency caused by phenylketonuria, if initiated early enough in life to prevent the disease's progressive effect on the developing brain.

Lofenalac is distinctive as an infant formula product in that it provides both a low phenylalanine content for control of the disease and also a balanced group of dietary nutrients needed for normal growth and development. Its protein component is a special casein hydrolysate from which most of the phenylalanine has been removed.

Aminopyrine

Aminopyrine according to L. Cardon et al. (*Ann. Int. Med.* 48:616, 1958) is of value particularly in conditions not amenable to therapy with specific chemotherapeutic and antibiotic agents or in patients in whom other antipyretics are not tolerated or in whom they have failed, or in patients in whom it is not advisable to assume the risks of therapy with corticotropin and the corticosteroids or in whom these agents have failed. Aminopyrine is still a uniquely valuable and occasionally a lifesaving antipyretic which deserves a trial whenever fever is a significant feature of the clinical picture of the disease. The danger of granulocytopenia from the use of aminopyrine, although real, has been overemphasized and is no greater than from many other drugs in common use today. Aminopyrine has its place in therapeutics under well-controlled clinical conditions and under supervision of a physician, but its careless and indiscriminate use is to be condemned.

New Leprosy Compound

A new treatment for leprosy was tested on 167 patients in Nigeria by T. F. Davey (*Leprosy Review*, January, 1958). It was BDPT (4 butoxy-4'dimethylaminodiphenyl thiourea) and appeared to combine freedom from toxic side-effects with a high therapeutic effectiveness. Its activity is as great as that of the sulfones and sometimes surpasses it. After 32 months of observation there was no evidence of the development of drug resistance. Drug hypersensitivity and psychosis were not encountered. On the basis of the experience so far, BDPT is considered to be the drug of choice when an alternative is needed to the sulfones. It can be combined safely with both sulfones and isoniazid and is particularly valuable in treating children. For large scale use BDPT dosage is relatively large, and, apart from its inconvenience, this adds to the cost of treatment.

Vesprin (Squibb) is triflupromazine hydrochloride, a new phenothiazine derivative for use in the treatment of certain psychoses. It is available as oral tablets of 10 mg., 25 mg. and 50 mg. in bottles of 50 and 500 and in parenteral solution in 1 cc. ampoules (20 mg./cc.)

Panalba KM (Upjohn) flavored granules combine tetracycline with novobiocin and potassium metaphosphate in an orange-mint flavored suspension when mixed with water. Each teaspoonful contains tetracyclent equivalent to 125 mg. of the hydrochloride, 62.5 mg. of novobiocin calcium and 100 mg. of potassium metaphosphate.

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Compounder's Corner

Heat-Stable Emulsions

When a given system of emulsifiers of known compositions and molecular weights was employed, W. S. Singleton et al. (J. Am. Oil Chem. Soc. 35:265, 1958) found that in order for fat emulsions of 15 per cent oil content to be stable to the heat required for sterilization, the emulsifiers must meet definite requirements. Minimum weight percentage of total lipophilic groups should be 0.29 per cent; minimum weight percentage of total hydrophilic groups should be 0.57 per cent; the polyoxyethylene groups of emulsifiers containing such groups should account for at least 70 per cent of the mole weight of these emulsifiers; the lipophilic/hydrophilic ratio should be about 0.5. The minimum content of lipophilic and hydrophilic groups was found to be an additive total of these groups as provided by the complete emulsifying system whether composed of individual or multiple emulsifying agents and whether of similar or dissimilar functional groups.

With the emulsifiers used, an acyl group greater in length than 12 carbon atoms was found to be necessary to prepare cottonseed oil emulsions which were stable to heat.

Resistance of emulsions to breakage by mechanical shock was imparted by a rather large amount of lipophilic groups, so that the lipophilic/hydrophilic ratio was 1 or over.

Egg Shampoo Labelling

The FDA has issued a statement clarifying its stand on the subject of the concentration of eggs required in egg shampoos.

"(a) An article designated as 'egg shampoo' should contain one egg (or the equivalent amount of dried whole egg) in that quantity of the article which would be used in one shampooing of the hair.

"(b) An article that contains less than one egg per 'shampoo' should not be referred to as an 'egg shampoo,' and the word 'egg' should not be used as part of the name of the article. At the present time, the Administration is not raising objection to the marketing of an article containing less than one egg per 'shampoo' provided the word 'egg' does not appear in the name of the article, the reference to the egg ingredient, such as 'plus egg,' appears in a subordinate position on the label and is in type which is substantially reduced in size in comparison with the title of the article, and the reference to the presence of egg reveals the amount of the egg ingredient.

"(c) In the case of an article containing less than 2 per cent egg, the amount of egg is so small as to be insignificant, and it is therefore considered that it would be misleading for the labeling to make any mention of the presence of egg in such a product."

Sucrose Acetate Isobutyrate

Sucrose Acetate Isobutyrate is being offered for investigation by Eastman Chemical Products, Inc., Kingsport, Tennessee and the enumerated properties certainly suggest usefulness in hair setting and hair dressing products in regular and aerosol formulations. According to the company's statements the new chemical, SAIB, has characteristics between those of a plasticizer and a resin. It is a clear, extremely viscous liquid, very stable to heat and water. The 100 per cent material is practically a semi-solid (100,000 cps.) at 30°C. but viscosity drops rapidly to 4,800 cps. at 50° and to 90 at 100°. SAIB-90 is a mixture of 90 per cent of SAIB and 10 per cent of ethyl alcohol with a room temperature viscosity of 750 cps. SAIB is compatible with a wide range of resins, plasticizers, oils and waxes; in solvent coating formulations it serves to extend solids content without significantly affecting the ultimate physical properties of the film. No mention is made of toxicity, which ought to be low. It is practically insoluble in water. Occlusive agent for skin moisture retention, bromo acid solvent and lipstick component, additive to hand and skin lotions and creams? The new compound ought to repay investigation for cosmetic and dermatologic application.

Chemical Disinfection

To carry out chemical disinfection properly one must know the principles that control it. The first is that strong chemical solutions kill microorganisms by coagulating the protein contained in them. Therefore, they act the same way heat does, and just as a high temperature is more rapidly bactericidal than a lower temperature so a strong concentration kills more quickly than a weak one.

This point leads us to the second principle which is that the inherent capacity of disinfectants to damage materials limits their maximum usable concentration.

On the other hand, a quaternary ammonium compound is a disinfectant because it is actively bactericidal in a concentration which does not damage inanimate objects. The third and most important principle is that the time required for complete disinfection depends upon three factors: (1) the nature of the object or material being disinfected; (2) the nature of the contamination; (3) the effectiveness of the chemical as a cidal agent.

It is an obvious fact that some objects can be disinfected more rapidly than others. The easiest type of surface is a flat, smooth, hard surface such as a scalpel or table top; porous and uneven surfaces, on the other hand, require good penetration, a general property of gases and of liquids with low surface tension.

The second factor affecting the disinfection time is the nature of the microbial contamination; in other words, the make-up of the microbial

population which must be destroyed. There are two aspects to this, the total number or population size and the types of microorganisms in that population. For purposes of chemical disinfection, bacteria fall into three classes with increasing resistance in the order given: (1) nonsporulating, vegetative bacteria such as staphylococcus, streptococcus and *E. coli*; (2) the tubercle bacillus; and (3) spores. The different between (1) and (2) is not great, but that between (1) and (3) is enormous. For example, the vegetative form of the tetanus bacillus is destroyed within a few seconds by a chemical solution that fails to kill the spores in days or even weeks of exposure. Very few chemicals or combinations of chemicals can kill spores in a length of time that is practical. Therefore, disinfection does not include the destruction of spores. Indeed, the exceptional chemical, either liquid or gaseous, with this power should be called a sporicide, and it may be used with the expectation of obtaining sterility.

Hundreds of different germicidal chemicals have been made available and some are better than others. The most useful types of germicides are listed below.

Mercurials. The commonly used mercurials are the bichloride and cyanide compounds. They are poor germicides and there is no place for them in modern disinfection.

Phenolics. In the 1 to 3 per cent concentrations recommended as the use dilution they are good germicides for floors, walls and furniture because of their tuberculocidal and virucidal activities. They are fairly active tuberculocides, but they are not sporicides.

Chlorines. Hypochlorites are good disinfectants for floors but not for instruments, which they corrode.

Iodine. The germicidal action is good, but its usefulness is limited by the fact that it stains most everything it touches. In combination with alcohol, 0.5 to 1.0 per cent iodine is a good tuberculocide for disinfection of oral thermometers. An iodine-detergent combination, is an improvement in that it does not stain, and it can kill tubercle bacilli if used in sufficient concentration (450 ppm. of available iodine). It is not a very good sporicide.

"Quats." This is chemical slang for a very large group of compounds having soap-like properties. Zephiran is the best known of the "quat" or cationic detergent germicides. The killing action for ordinary vegetative bacteria is very good, but there is no effect on the tubercle bacillus, and virucidal activity is limited. On the other hand, aqueous Zephiran has the virtue of being non-irritating in the 1:1000 concentration generally used.

Alcohols. The germicidal power of ethyl and isopropyl alcohol is generally underrated. Not only are vegetative bacteria destroyed very rapidly by 70 to 95 per cent concentrations, but so also is the tubercle bacillus. Indeed, alcohol appears to be the tuberculocidal agent of choice, and, when combined with other chemicals, it increases the germicidal effect. It is not sporicidal.

Formaldehyde. A strong aqueous solution (8 per cent formaldehyde or 20 per cent formalin) is a disinfectant and even a sporicide. When combined with alcohol the action is even greater. Both the tubercle bacillus and viruses are promptly killed. This combination is the most germicidal solution commonly available.

This discussion has been based on the principle that strong disinfectant solutions can act rapidly. Weak solutions can also kill bacteria in slower and more subtle ways. Absorption of some chemicals upon the bacterial cell results in blocking essential enzyme systems, a process that eventually will result in death by starvation unless the chemical is washed off or neutralized. This is death by bacteriostasis, and mercurial compounds work this way. — E. H. Spaulding, Becton-Dickenson Lecture

Measuring Fat and Wax Hardness

Heretofore a good method for measuring the hardness of fats and waxes has not been available. Instruments currently used to measure hardness (not consistency) are relatively inaccurate and give results based on an arbitrary scale.

A new instrument and technique has been devised by N. V. Lovgren, W. A. Guice and R. O. Feuge (*J. Am. Oil Chem. Soc.* 35:327, 1958) for measuring the hardness of fats and waxes. They are essentially an adaptation of the Brinell hardness test used for metal and alloys. In determining the hardness of a fat or wax, a perfectly round steel ball having a diameter as small as 0.1250 in. or as large as 0.5000 in. is pressed with a force of 200 g. to about 6 kg. onto the surface being tested. The hardness index, in terms of kilograms per square centimeter, is determined from the slight impression produced. The index is relatively independent of ball size, test load, and other test conditions, provided these are confined to certain ranges.

Hardness indices have been determined for products ranging from poorly tempered cocoa butter to rosin. Differences in hardness observed have varied over 1500-fold. The hardness of cocoa butter has been found to vary over seven-fold, depending on thermal history.

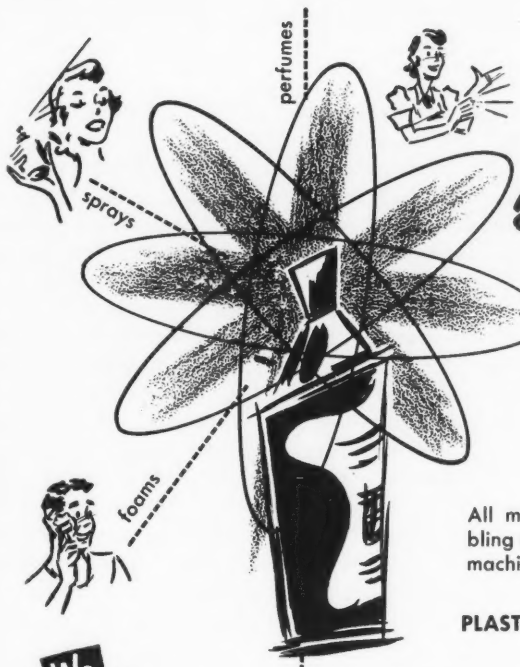
Synthetic Cocoa Butter

Technical considerations indicate that cocoa butter-like mixtures can be prepared readily by the esterification of mixtures of oleic, palmitic, and stearic acids, or the interesterification of their glycerides, followed by the fractional crystallization of the reaction products.

Using the indicated procedures, three cocoa butter-like fractions were prepared by R. O. Feuge, N. V. Lovgren, H. B. Cosler (*J. Am. Oil Chem. Soc.* 35:194, 1958). One consisted essentially of oleopalmitostearins, another consisted essentially of oleodistearins, while the third consisted mostly of oleodipalmitins.

On the basis of softening point curves, the oleopalmitostearin product was most compatible with cocoa butter, the oleodistearin product was the next most compatible, while the oleodipalmitin product was least compatible. When mixed with cocoa butter, all three of the products produced consistency *vs.* temperature curves whose shapes closely resembled that of cocoa butter. All of the mixtures softened over a short temperature interval though the actual temperature at which softening occurred varied. The several products are believed to be satisfactory cocoa butter replacements.

Another cocoa butter-like fat was prepared by the interesterification of 70 parts of completely hydrogenated cottonseed oil and 30 parts of olive oil and the subsequent fractionation of the reaction product.



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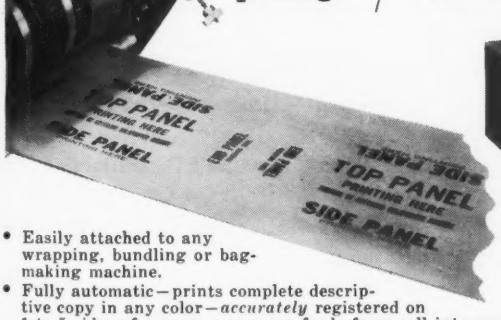

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ardization of adsorbents and of the technique employed are important in order to obtain reproducible results.

Moncrieff explains the use of his apparatus in the following language:

"In utilizing the apparatus of the invention, air is passed through the system picking up odorant and carrying the mixture through the adsorbent material at a low rate, and under such conditions, assuming that the adsorbent will take up even small amounts of the odorant, none of the odorant will be present in the vapors discharged from the adsorbent. The rate of air flow is then gradually increased until a trace of odor is first detected in the discharging vapors. This point can be determined by the operator (or another) sniffing the discharged vapors or possibly by physical or chemical detecting means. The point at which odorant first is recognizable in the discharge vapors is the end point of the test, and reading the rate of air flow in cc./sec. and knowing the length and cross-sectional area of the adsorbent bed the critical contact time in seconds is readily calculated using the foregoing formula."

While any materials having adsorbent properties are potentially useful, Moncrieff has selected the following: activated charcoal, silica gel, activated alumina, activated fuller's earth, and vegetable fat supported on a carrier.

RECENT PATENTS

2,819,314—Ortho Pharmaceutical—Vitamin A-Related Compounds.

2,819,315—Upjohn — 5-Benzyloxy-β-2-Dinitrostyrenes.

2,819,318—Ethyl Corp.—Alcohols Derived From Babassu Oil

2,819,998—Chas. Pfizer—Quat. Salt Derivatives of Harman.

2,819,999—Novo Terapeutisk Lab. (Denmark)—Crystallization of Insulin.

2,820,000—A. Menzies — Dentifrice Comprising Diatomaceous Silica.

2,820,030—Glidden—16, 17-Oxido-Steroids of the C_{21} Series.

2,820,035—C. H. Boehringer (Germany)—Barbituric Acid Derivatives.

2,820,038—Ciba—2-Diphenyl-Methyl-Piperidine

2,820,039 — Parke, Davis— 1-(γ-Butoxyphenyl)-3-(γ-Pyridylphenyl)-2-Thioureas.

2,820,040—Chas. Pfizer—Substituted Mono-Ammonium Salts.

2,820,042—Schenley—(Dialkylaminoalkylthio) Benzoxazoles.

Skin Research

Cosmetic Dermatitis

The yearly incidence and distribution of dermatitis due to hair dye, lipstick, nail lacquer and cold permanent wave lotion was evaluated by F. Reiss of New York (*Dermatologica* 116:419, 1958) on the basis of 956 answers to a questionnaire sent to 2969 American dermatologists and allergists. These reported a total of 14,897 cases of observed dermatitis due to these cosmetics, 58 per cent of which were confirmed by patch test.

The largest number, 36.6 per cent of the cases of allergic manifestations due to the four cosmetics, was caused by nail lacquer.

The comparatively infrequently applied cold permanent wave solution represented 25.2 per cent of the total reported dermatitis. However, it should be noted that dermatitis caused by a permanent wave solution was due to chemical irritation. In many of the answers clear information was given that the cold permanent wave solution acted as primary irritant and caused chemical burns and breakage of hair.

The widely and frequently used lipstick was responsible for only 14.6 per cent of the total reported cases.

Hair dyes were responsible for only 23.8 per cent of the allergies reported. This was astonishing, as in general, hair dyes are incriminated as the main cause of cosmetic allergic sensitization. The low number of allergic reactions caused by hair dyes, notwithstanding cross-sensitization, must be attributed to the more general use of the patch test by the hairdressers and the public, and improved formulation of the product. A large number of nationally recognized dermatologists emphasized in their additional remarks the recent scarcity of hair dye allergies as compared with previous years.

The conclusions derived from the questionnaire confirm the practical value of the patch test, which was widely used for diagnostic purposes.

In additional voluntary information, many dermatologists commented on the frequency of allergies due to deodorants and detergents. Some considered this more frequent than that due to the four cosmetics in question. Remarks on a limited number of allergies due to hair lacquer was also made. However, special emphasis was placed on deodorants as the principal cause of contact dermatitis.

The remote possibility of causal relationship between blood-dyscrasias and cosmetics was also raised.

Among the 951 dermatologists only four reported observations of this nature. In all instances the symptoms promptly disappeared after discontinuation of the incriminated cosmetics.

Glycyrrhetinic Acid

E. Colin-Jones and G. F. Somers. (*Med Press.* 1957, 238, 206.) review the pharmacology of glycyrrhetinic acid and report on its anti-inflammatory activity as evidenced by tests on experimental animals and an extensive clinical investigation in a variety of skin diseases. Glycyrrhetinic acid is a complex triterpene derived from glycyrrhizic acid, the sweet constituent of licorice. The authors have demonstrated the anti-inflammatory action of the biologically active isomers of glycyrrhetinic acid in established experimental methods in laboratory animals. It is also reported that it heals experimentally induced inflammatory lesions on the skin of the rabbit and reduces induced inflammation in the rabbit eye. Clinically, the topical application of ointments containing the active isomers of glycyrrhetinic acid in 254 cases has shown its value in a variety of dermatological conditions. In a comparison with hydrocortisone ointments it compared favorably in subacute and chronic conditions. The ointment was found to be most effective in flexnural eczema, traumatic and contact dermatitis, napex neurodermatitis, disseminated neurodermatitis, pruritus associated with psoriasis and in pustular psoriasis. Some value was found in infantile eczema, nummular eczema and in pruritis vulvae and ani. Glycyrrhetinic acid has been shown to act synergistically with the antibiotic neomycin, giving excellent results in impetigo and impetiginised eczema. In psoriasis the depressive action of glycyrrhetinic acid on the inflammatory process, combined with the antieczematous action of tar and the keratolytic action of salicylic acid gave more effective and speedier results than any of these used alone. The active form of glycyrrhetinic acid brought relief in cases which had hitherto been intractable to other forms of treatment. It was concluded that certain fractions of the acid have a marked anti-inflammatory action and were effective in a variety of skin diseases, and compared favorably in subacute and chronic conditions, with hydrocortisone.

Comment: According to the latest edition of the U. S. Dispensatory, licorice root contains 5 to 10 per cent of the characteristic principle glycyrrhizin or glycyrrhizic acid as the potassium and calcium salts. This is a glycoside which on hydrolysis yields 2 molecules of glucuronic acid and one molecule of glycyrrhetinic or glycyrrhetic acid, a pentacyclic terpene. Cosmetic as well as dermatologic investigators might well explore the possibilities of this compound as an over-the-counter antiinflammatory agent.

Seborrhea Capitis Treatment

The four elements, oxygen, sulfur, selenium, and tellurium, are generally known to be related in their chemical properties. Additionally, it has been demonstrated that sulfur and selenium possess related therapeutic properties which are of particular value to the dermatologist in his treatment of seborrhea capitis. It was deemed wise to assume that compounds of tellurium might have similar therapeutic application.

During the past four years a standard 2.5 per cent suspension of tellurium dioxide in a suitable shampoo vehicle has been used in intensive clinical studies by E. R. Gross and C. S. Wright (*A.M.A. Arch. Dermatol.* 78: 92, 1958). Safety tests were carried out on laboratory animals, and excretion studies on human urine were made by determining the tellurium content before and after treatment with tellurium dioxide shampoo.

There was no indication of skin irritation or of pathological change in the animal organs, and blood smears failed to show pathological variation.

Spectographic determinations were made on six samples of urine before and after patients' use of 2.5 per cent tellurium dioxide suspension as a shampoo. "Control samples run at the same time, in identical manner, to which known amounts of tellurium were added, gave distinct spectrum lines down to concentrations of 2 ppm. As no tellurium lines were obtained in any of the . . . samples we are reporting the tellurium as less than our lowest standard."

Wright reviewed 159 case histories of patients who were using 2.5 per cent tellurium dioxide suspension shampoo over a period of three years for the treatment of seborrhea capitis. He reported the following results: 69 cases completely controlled; 72 cases improved; 18 cases unimproved. He stated that the average frequency of application in seborrhea oleosa was 4 to 7 days and that in seborrhea sicca it was 14 to 20 days.

He was particularly impressed by the simplicity of application, since no other soap was needed. In his series there were no untoward reactions and no formation of oiliness on the scalp.

Gross observed 83 patients who were using the 2.5 per cent tellurium dioxide suspension shampoo over a period of four years and reports that 60 were able to control their seborrhea; 10 patients were improved, and 13 were unimproved. There were no complaints of increased oiliness of the scalp. The tellurium shampoo produced no unfavorable reactions and was cosmetically acceptable to all patients, particularly in its ease of application as compared with other medicated shampoos employing this group of elements.

Bolus, in 1954, observed 26 patients undergoing treamtent with tellurium suspension for seborrhea capitis for varying periods ranging from one to six months and noted that all patients showed marked improvement and were able to control their seborrhea. He reported no unfavorable sequellae.

In January, 1954, E. W. Kieck reported on eight patients achieving excellent control of their seborrhea capitis through the use of tellurium dioxide shampoo.

Leon Goldman, in January, 1956, briefly summarized his clinical studies of tellurium dioxide shampoo by reporting that there were no staining effect on the hair; no accentuation of scalp oiliness, as with selenium compounds, and an absence of hydrogen sulfide odor. He observed no irritation in his group of patients and considers it a good medicated shampoo.

—Comment: This pretty well disposes of the sixth periodic group, the first member, oxygen, being an unsable gas and the last member, polonium, too radioactive. Now it remains to derive relationships, perhaps oxidation-reduction in the cystine-cysteine system, that will permit extension not only to polythionates (as in Theradan) but also into suitable organic compounds of reduced toxicity.

Sugar Ointment

Sugar paste has been used in the past for ulcers, but it is new in the sense that most dermatologists are unaware of it, and it has not been written up in the dermatologic literature. The formula of the paste is powdered cane sugar, 30 gm., wool fat (anhydrous lanolin), 60 gm., and compound benzoin tincture, 2 cc.

A. Rostenberg, E. Wassermann and R. S. Medansky (*A.M.A. Arch. Dermatol.* 78: 94, 1958) treated 19 persons, 8 men and 11 women, whose ages ranged between 50 and 76. The diagnoses were as follows: stasis ulcers 12, trophic and/or decubitus ulcers 4, sclerodermatous ulcers 1, radiation ulcer 1, ulceration associated with mixed peripheral vascular disease 1. The average duration of the ulcers prior to sugar therapy was one year. In nine patients the ulcers healed completely. In four persons with stasis ulcer there was improvement of varying degree but not complete healing. The three persons with ulcers associated with scleroderma, radiation, and mixed peripheral vascular disease did not obtain any improvement. In general, improvement was noted in one to two weeks, and in the ulcers which healed completely took on the average about three months. Four patients complained of some pruritus and burning in the tissue surrounding the ulcer which was of a rather mild degree and in no case necessitated interruption of the therapy. The paste was applied twice daily. In addition to the cases included in this report, there were personal reports from several physicians who have treated other patients with the paste, with, on the whole, favorable results.

The authors have done no studies which would furnish any basis for understanding the mechanism by which the sugar paste works.

Onycho-Phytex (Wynlit) is a topical therapy for nail fungus infections. The preparation contains a complex made from 46 mg. of tannic acid and 29 mg. of boric acid, 8 mg. of salicylic acid and 56 per cent of ethyl alcohol. It is supplied in 30 cc. bottles.

Rhusticon (American Pharmaceutical) is a washable lotion containing zirconium hydroxide, titanium dioxide, benzocaine, pyrilamine maleate and tyrothricin to prevent, neutralize and relieve the toxic action of poison ivy, oak or sumac. The preparation is sold in 3 ounce bottles.

Capsebon (Pitman-Moore) is a one per cent cadmium sulfide suspension in a shampoo base for the treatment of seborrheic dermatitis.

(*Continued from page 157*)

Toxicity of Kanamycin in man is of minimal order according to P. A. Bunn et al. when from 0.5 to 3 grams daily are administered intramuscularly for periods less than three weeks. When given for longer periods, four untoward side reactions are observed: eosinophilia in the majority, abnormalities of urinary sediment, some soreness at site of injection and, usually after 50 grams or more have been given, hearing loss.

Blood levels and urine excretion studies in man indicate that little absorption from the intestinal tract takes place. Following intramuscular administration. rapid and high peak concentrations are attained in serum and there is rapid elimination in urine.

Some 35 patients with acute infections have been treated. Impressive responses in 20 patients with staphylococcal infections have been observed. Infections caused by Proteus, aerobacter and *E. Coli* bacteria have been favorably altered. A few infections caused by pyocyaneus have not been benefitted by Kanamycin.

W. L. Hewitt and S. M. Finegold found that kanamycin had a broad spectrum with good activity vs. staphylococci, *E. Coli* and Klebsiella aerobacter. Various strains of Proteus representing all species and several Salmonella strains were either weakly or moderately sensitive to kanamycin. Pseudomonas, Alcaligenes and enterococci were relatively or highly resistant.

Five strains of *Coccidiodes immitis* were resistant to at least 50 mcg./ml. of kanamycin.

Five patients received 6 gm. of kanamycin orally per day (with an extra 3 to 4 gm. loading dose the first day) while eating their usual hospital diet; all aerobic bacteria were eliminated in each case—usually within 24 to 72 hours. Bacteroides persisted in large numers in all patients, but the effect on other anaerobes (Clostridia, Lactobacillaceae) was variable.

Two patients receiving 1.5 gm. of kanamycin intramuscularly daily were studied for changes in fecal microflora. Results suggest that relatively little kanamycin reaches the lower bowel in active form after intramuscular therapy.

During the six-month period from January 1958 to June 1958, seventy-six cases of bacterial infection were treated by F. G. Davies with Kanamycin at the Marcy State Hospital, Marcy, New York

The dosage of the drug varied with the severity of the infection but the average was 1 to 2 gm. a day usually given as 0.25 gm. i.m. q.i.d., or 0.5 gm. i.m. q. i. d. The average duration of treatment was 10 to 14 days.

Thirty-seven cases of furunculosis healed with one course of treatment. The two decubitus ulcers healed slowly over a two to three month period. The cases of otitis media completely cleared after there had been no improvement with other antibiotics. There was complete healing of the six cases of cellulitis of the skin. The cases of urinary tract infection, bronchopneumonia, paronychia, varicose ulcer of the leg, and one case of staphylococcal gastroenteritis responded well to Kanamycin. Sixteen typhoid carriers were studied. Ten of these patients had negative stool cultures after two weeks of therapy. Most of these infections had been treated previously with other antibiotics without effect, but responded to Kanamycin.

Minimal toxic effects were found. The most frequent complaint was mild pain at the site of injection.

Initial studies concerning kanamycin suggested to S. Berger and F. Wehrle that it might be useful in certain infections involving infants and children. This seemed particularly true of infections due to penicillin resistant staphlococci.

Kanamycin is rapidly absorbed following intramascular injection in children, and there is no evidence of local tissue intolerance. Administration of doses at least as frequently as at 6-hour intervals will probably be required for sustained serum levels in the therapeutic range.

Kanamycin therapy has been initiated or completed in 20 patients by C. R. Kleeman et al. Twelve have received this drug for periods varying from 7 to 30 days with a mean duration of 20 days. In 8 of the 12 patients the dosage schedule was 50 mg./kilo/day, the rest received 25 mg./kilo. These patients received this antibiotic for the treatment of infections considered within its spectrum.

Results are very incomplete and do not represent a final evaluation of this drug on renal function. However, they do suggest that a slight decrease in glomerular filtration rate and tubular function may occur in approximately 30 per cent of cases. The reversibility of these changes have been investigated to date.

Experience covering six months on patients ranging in ages from 40 to 67 years was reported by K. W. Wright et al. With the exception of two patients, all had organisms initially sensitive to less than 10 mcg./ml. kanamycin *in vitro.*

The patients had disease which, in most cases, was not expected to show significant improvement. All organisms were resistant to the usual antituberculous agents.

Toxic manifestations, the appearance of granular casts and 8th cranial nerve damage, were reported. Eosinophilia was common.

An antituberculous effect judged to be greater than would be expected from bed rest alone is demonstrated by some patients. Organisms from all the patients became resistant to greater than 100 mcg./ml. by 120 days and in one-half the patients by 60 days.

The long-term administration of kanamycin in 0.5 gm. daily dose under controlled conditions is feasible; it warrants further trial and may be useful in the treatment of some patients with tuberculosis and possibly in treatment of diseases associated with atypical

(*Continued on page 249*)

(*Continued from page 159*)

ceiling presents a smooth unbroken appearance with not even the lighting conduits exposed, these having been buried in the roof during construction. The center of each bay is about 25 feet high and approximately fifteen feet at the column lines. Downspouts from the roof form the cores of the small concrete supporting columns, which are only fourteen inches in diameter. The clutter of pipes, trusses, struts and sway braces usually visible on the ceiling of the average pharmaceutical plant is eliminated.

Because labor in Mexico is so much cheaper than in the U. S., it was decided to bring services lines to equipment in floor ducts. These ducts were gridded so closely that the usual inflexibility encountered by a fixed service grid is not and will not be encountered. The only overhead service lines that are visible are the dust collection hoods and ducts from various pieces of equipment. These could not have been eliminated and still accomplish the exceptional standard of plant sanitation that the management established and is maintaining.

The plant utilizes a combination of window and roof lighting. Windows are provided around the entire perimeter of the factory and warehouse section. The arches under the convolute roof over the office section are fitted with windows, and, since the factory section is so much higher than the personnel section, windows are also provided above that section too. The result is that daylight floods into the factory and warehouse areas from all four sides and from the roof as well. In the center of the vaulted roof above each bay there are some lucite bubbles to admit daylight from above. The result is that Colliere has a factory so well-lighted that fine print can be read anywhere in the factory or warehouse without eyestrain and without supplementary artificial light.

The acceptance by the writer of roof lighting will surprise many readers who know his antipathy to all and every form of roof lighting. These objections have been stated in detail elsewhere and are all based on high U. S. construction costs, high maintenance costs and high heating and cooling costs. If our stupid building codes permitted the construction of lightweight convolute roofs I'd be for roof lighting in the form of plastic bubbles such as Colliere uses. They are flexible and will not crack with expansion and contraction. Neither will the roof itself. It also is flexible. A convolute roof made of reinforced vermiculite concrete only 3 inches thick at the apex, and covered with the usual tar and gravel roof finish, will support a live load of 75 pounds per square foot. Even among the northern tier of states, very few require a snow load as high as this. But the codes, most of them written fifty or more years ago, will not yet permit the use of such practical and economical construction. Also, few of our contractors know how to build a lightweight convolute roof. It is a bit tricky.

The factory and warehouse section is laid out in three parallel areas all parallel with personnel service service wing. The first one next to the personnel service area contains those rooms which had to be partitioned because of the nature of the work done in them such as air conditioned rooms, biological laboratories and control laboratories. This section is designed to expand in the same direction as the personnel wing.

The next and principal section is the manufacturing and packaging area. With the exception of a few specialized rooms that had to be partitioned, this area is wide open and dependence is placed on good dust collection equipment, rigid supervision and sanitary procedures. The factory is spotless.

Processed materials after being released by the control laboratories flow directly into packaging. Because of the wide range of Colliere products and small batch sizes, packaging necessarily is performed on hand lines, semi-automatic lines and one partially automatic liquid line. The entire plant is palletized as much as possible.

Finished products flow from the packaging department into a detention area where they are held for requisition by the finished stock department. Deliveries are made by full pallet load to the finished stock department and are then considered sold. This enables the accounting department to make up monthly statements quickly without having to wait until inventories are taken. Reconciliation of all inventories in the detention area and in the shelf stock area is made annually when a detailed physical inventory is then taken. The shelf stock area feeds the packing and shipping department from which outgoing orders flow to a common receiving and shipping platform.

Incoming materials received on this platform are transported to the raw material and packaging sections of the warehouse area. As requisitions are made in the warehouse, materials are delivered to the manufacturing and packaging departments, respectively. Hence, the flow of materials from the warehouse through processing and packaging departments forms a C. The factory is designed so that it can be expanded without disruption directly into the warehouse area and the warehouse area can be expanded without confusion or conflict as future requirements dictate.

Mr. Bernard Colliere, president of the company, is very much in favor of this type of one story building and this type of layout. The first plant designed by the writer utilizing this type of layout was built in Santiago, Chile, in the late forties. When in the ensuing years the plant had to be expanded, it was done with no interruption of operations. Subsequently, when the company built a plant in Lima, Peru, exactly the same layout was used again, although the architecture is different. The Mexican plant is big brother to the other two in layout and in operation. Thus, one firm utilized a type of layout I have long

(*Continued on page 232*)

Trade Literature

Archer-Daniels-Midland

The Chemical Products Division, Archer-Daniels-Midland Company, Box 839, Minneapolis 40, Minnesota, has published a new 52-page catalog of its line of aliphatic chemicals. Included are test data on ADM's olefins, hydrocarbons, fatty alcohols, hydrogenated and vegetable fatty acids, glycerides and sperm oil products. Also included is the first commercial presentation of gas chromatographic composition data on olefins, hydrocarbons, fatty alcohols, and hydrogenated fatty acids. Solubility, compatibility, compatibility, and physical constant charts are given for the various products.

Constant Temperature and Humidity

The J. O. Ross Engineering Division of Midland-Ross Corporation, 444 Madison Avenue, New York, offers a new four-page bulletin covering the Ross Constant Temperature and Humidity Control Unit for testing laboratories.

Molo-Jell

Special properties of Molo-Jell, a high smoke-point pressing oil used in hair preparations are analyzed in a bulletin (Current Topics No. 135) available from L. Sonneborn Sons, 304 Fourth Avenue, New York 10.

Ion Exchange

Ten methods of ion exchange regeneration are discussed in Technical Reprint T-159 available from Graver Water Conditioning Co., 216 West 14 Street, New York 11.

Acetylene Chemicals

A technical brochure outlining the properties and uses of high-pressure acetylene derivatives is available from Antara Chemicals, 435 Hudson Street, New York 14. Applications of these chemicals for a host of products including pharmaceuticals and cosmetics are featured. The structural and physical forms of eleven high-pressure acetylene derivatives, which are offered in commercial quantities, are included.

Gas Chromatography

A new, descriptive 24-page notebook on Gas Chromatography, complete with photographs, graphs, and traces is available from Wilkens Instrument & Research, Inc., Walnut Creek, California. In addition to listing specifications and prices for three Aerograph models with columns, column packings, micro syringes, recorders, and other valuable accessories, the booklet demonstrates techniques on fatty acids and terpine analysis, showing Aerograph traces on a number of the more difficult separations.

Adipic Acid

National Aniline Division, Allied Chemical Corporation, 40 Rector Street, New York 6, has issued Technical Bulletin I-12R—Adipic Acid—which has been completely revised and expended to include comprehensive current information on this widely-useful reactive dicarboxylic acid. This 36-page booklet includes physical properties, 6 pages of chemical properties and reactions, 19 pages of suggested uses, and a list of 271 literature references.

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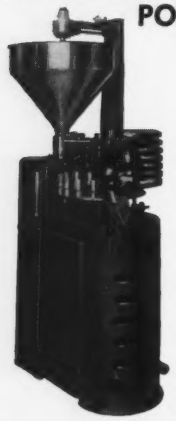

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advocated and it has been proved out in three different size plants in three different countries. I have used the same type of layout several times in this country and in several countries throughout the world, in plants both much larger and much smaller than the Colliere plant, and it always works out very well.

Throughout the whole project I was impressed and encouraged by the wholehearted cooperation given me by Mr. Colliere and all his associates at all levels. It is a fine, well managed, efficient organization. The entire project was so well planned and supervised that no extras were encountered and the contractor's final price was exactly his original bid. And the contractor's price for a really first-class job was about one-third of what it would cost to build a similar building in this country.

SOLUBILIZATION

(*Continued from page 161*)

referred to throughout the paper as E.O.

Table II (p. 234) summarizes the analytical data on solubilizers compared in this study. It will be noted that the products vary considerably in hydroxyl number, saponification number, and to a lesser extent in iodine number. However, no correlation of these data with activity as solubilizers could be established, because the solubilizers and solubilizates of this study are not pure compounds.

Table III (p. 234) lists the several water-insoluble lanolin compounds which were included in this study as solubilizates.

TABLE I

LANOLIN DERIVATIVE SOLUBILIZERS

CODE NO.	
	ETHERS*
#8	8 MOLS. E.O. ON SELECTED LANOLIN ALCOHOLS
#16	16 " " " " " "
#20	20 " " " " " "
#28	28 " " " " " "
	ESTER-ETHERS
#20L	20 MOLS. E.O. ON LANOLIN
#97**	ACETYLATED E.O. DERIVATIVE (9 MOLS.) OF LANOLIN ALCOHOLS AND HYDROXYESTERS
#98**	PARTIALLY ACETYLATED E.O. DERIVATIVE (11 MOLS.) OF LANOLIN ALCOHOLS AND HYDROXYESTERS

*EXPERIMENTAL PRODUCTS, **SOLULAN 97, SOLULAN 98; AMERICAN CHOLESTEROL PRODUCTS, INC.

In view of the lanolin origin of the solubilizers, it was considered important to evaluate their effect on lanolin and water-insoluble lanolin derivatives. Since the amount of lanolin solubilizate is generally low with respect to solubilizer, the use of lanolin-derived solubilizers substantially fortifies the emollient lanolin effect.

Reader's Questions . . .

Topical Analgesic Preparations: *What is the basis of creams and similar preparations intended for the relief of muscular pain? Is a local anesthetic usually included in these mixtures and is there any clinical evidence that they are effective?* CHICAGO

Local anesthetics are only incidental ingredients in topical analgesics. Most important are irritants or rubefacients and percutaneous salicylates. A typical cream being promoted in Europe contains 7.5 per cent of benzocaine, 2.0 per cent of methyl nicotinate and 10.0 per cent of glycol salicylate. The benzocaine will deaden to some extent the area to which it is applied and give the illusion of pain relief; the nicotinic ester will cause subcutaneous reddening as a counterirritant; the glycol salicylate can undergo percutaneous absorption and act as a salicylate in the blood stream to relieve pain.

Needless to say, these active components or others related them, may be used in a variety of dosage forms, including sticks, creams, lotions or aerosols. Among the suggested ingredients have been dimethylamine salicylate, nonylic acid vanillamide, butoxyethyl nicotinate, capsicum oleoresin, balsam Peru, and epinephrin.

In a recent issue of the British medical publication "The Lancet", a correspondent described his controlled tests with three analgesic preparations. "In a strictly controlled bouble-blind investigation recently conducted, an adrenalin cream was compared with two rubefacient ointments containing nonylic acid vanillamide combined with butoxyethyl nicotinate and a combination of methyl nicotinate, glycol salicylate, histamine dihydrochloride and capsicum oleoresin. Fifty patients with degenerative joint disease of the spine were subjected to the trial. In only 9 of the trials were there measurable objective improvement and 3 of these resulted from the placebo. Subjectively, 21 patients preferred the vanillamide product, 11 the methyl nicotinate combination, 4 the adrenaline cream and 4 the inert cream."

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(*Continued from page 232*)

TABLE II

ANALYTICAL DATA ON LANOLIN DERIVATIVE SOLUBILIZERS

ETHERS	ACID NO.	SAP. NO.	OH NO.	I NO.	FORM	5% SOL. IN ABSOL.	5% SOL. IN ETHANOL 50%
#8	1.4	8.0	101	25.0	WAXY SOLID	CLEAR	HAZY
#16	1.6	6.1	62	17.3	WAXY SOLID	CLEAR	CLEAR
#20	0.5	10.2	59	14.9	WAXY SOLID	CLEAR	CLEAR
#28	0.6	2.9	49	13.8	WAXY SOLID	CLEAR	HAZY
ESTER-ETHERS							
#20L	0.6	24	29	14.2	WAXY SOLID	HAZY	HAZY
#97	1.0	117	3	18	OILY LIQUID	CLEAR	CLEAR
#98	0.5	68	64	19.4	OILY LIQUID	CLEAR	CLEAR

Procedure

A relatively simple technique was utilized in these experiments based on the preparation of mixtures of solubilizer (S) and solubilizate (Z) at fixed ratios to each other. These are herein referred to as S/Z mixtures and the ratios as S:Z ratios. Successive aqueous dilutions of the S/Z mixtures were prepared and observed visually over wide ranges of dilution for the degree of solubilization achieved by the individual

TABLE III

SOLUBILIZATES

LANOLIN (U.S.P.)

LIQUID LANOLIN (Viscolan™), AMERICAN CHOLESTEROL PRODUCTS, INC.

ACETYLATED LANOLIN (Modulan®), " " " "

ACETYLATED LANOLIN ALCOHOLS (Acetulan™), AMERICAN CHOLESTEROL PRODUCTS, INC.

LANOLIN ALCOHOLS LINOLEATE (Polylan™), " " " "

solubilizer-solubilizate combinations.

S:Z ratios of 9:1, 6:1 and 3:1 were selected for the preparation of the S/Z mixtures. Each solubilizer was combined with the individual solubilizates at the indicated ratios. Wherever necessary the S/Z mixtures were heated at approximately 80°C and mixed to achieve uniform dispersion.

Dilution of the mixtures with water was carried out in stepwise fashion. Earlier studies had demonstrated that it was not only convenient, but often advantageous for enhanced clarity, to first prepare a 1:1 dilution of the S/Z mixture with water. These 50 per cent aqueous solutions of each S/Z mixture were then heated for 30 minutes at 80-90°C and shaken to insure uniformity of dilution. The solutions were allowed to stand for 24 hours at room temperature before proceeding with further dilution. They were next diluted 1:1 with water and heated for 30 minutes at 80-90°C, shaken, and allowed to stand for an additional 24 hours at room temperature. The resultant 25 per cent solutions of the S/Z mixtures were diluted in similar stepwise fashion, down to 3.13 per cent but without the 24 hour interval between dilutions. This completed a broad range of dilutions for observing the degree of solubilization of the materials at each of the three ratios. In most cases the viscosity of the 25 per cent and lower concentrations of S/Z mixtures permitted further dilution without heating. However, an occasional mixture required heat in preparing the 12.5 per cent solution. In these instances the solution was always cooled to room temperature before proceeding with further dilutions.

For convenience in handling the many samples involved, these experiments were carried out in 1 oz. jars, sealed to avoid water loss. Table IV presents a schematic summary of the procedure followed in the preparation of the 50 per cent solutions. The desired lower concentrations at all S:Z ratios were obtained by diluting 5 gm. aliquots of the 50 per cent solutions, serially.

TABLE IV

PREPARATION OF SOLUBILIZED SYSTEMS

S:Z RATIO	SOLUBILIZER +	SOLUBILIZATE +	H_2O ADDED TO MAKE 50% SOL. of S/Z MIX.
3:1	6.0 gms. +	2.0 gms. +	8 ml.
6:1	6.0 gms. +	1.0 gm. +	7 ml.
9:1	4.5 gms. +	0.5 gm. +	5 ml.

The appearance of the dilutions was noted after 72 hours. Samples were rated clear, opalescent and turbid. Recording opalescence was considered of experimental value since opalescence represents a high degree of solubilization.

Results

In assembling the data obtained in this study from almost a thousand test samples, it was necessary to devise a graphic form which would convey the mass of information in a readily interpretable manner. Figures 1 through 5 represent the appearance of the

TABLE V

SOLUBILIZATES

PERFUME #313 (VAN AMERINGEN HAEBLER)

• VANCIDE 89 RE (R.T. VANDERBILT CO.)

MINERAL OIL (70 VISCOSITY)

•• HEXACHLOROPHENE (SINDAR CORP.)

VITAMIN A PALMITATE (CHAS. PFIZER)

EXTRACT OF LANOLIN ALCOHOLS (AMERCHOL L-101, AMERICAN CHOLESTEROL PROD. INC.)

• 2% SOLUTION IN ACETYLATED LANOLIN ALCOHOLS.

•• PROPYLENE GLYCOL ADDED AS A CO-SOLVENT.

various concentrations of S/Z mixtures in water. Each vertical column on the graph represents a different ratio of solubilizer to solubilizate. The concentration of the mixture of solubilizer and solubilizate.

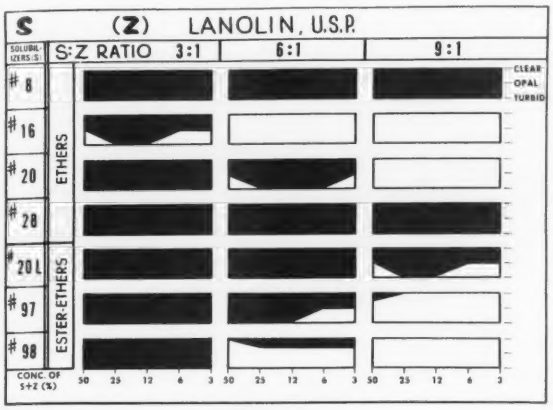

Figure 1

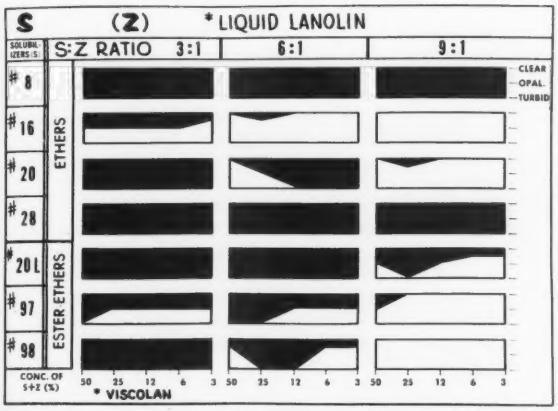

Figure 2

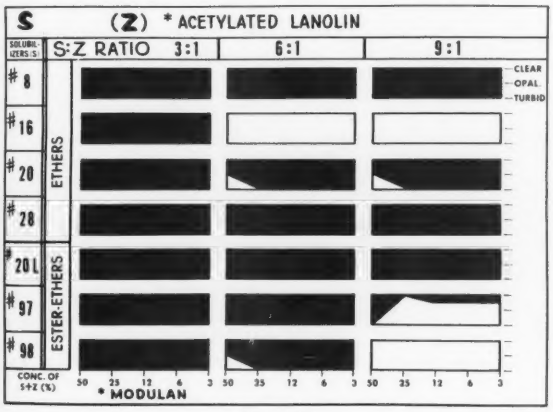

Figure 3

(S+Z) in solution is marked in per cent at the bottom line of each column; five concentrations being recorded in each case. Dark areas represent turbidity or failure. Various degrees of clarity and opalescence are depicted by the height of the clear area. An example of a crystal clear solution would be the 6 per cent concentration of lanolin and solubilizer #97 at a ratio of

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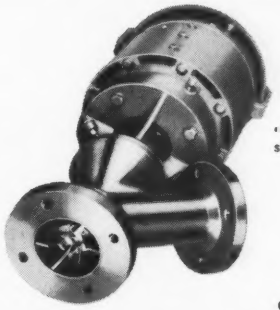
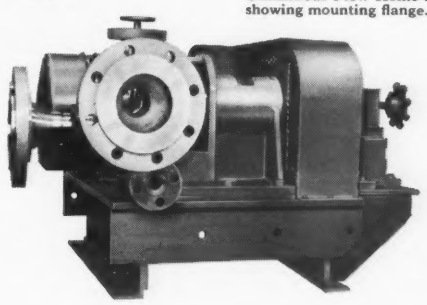


"Pipe-Line" Homo-Mixer showing intake turbine.

Continuous Flow Homo-Mixer showing mounting flange.



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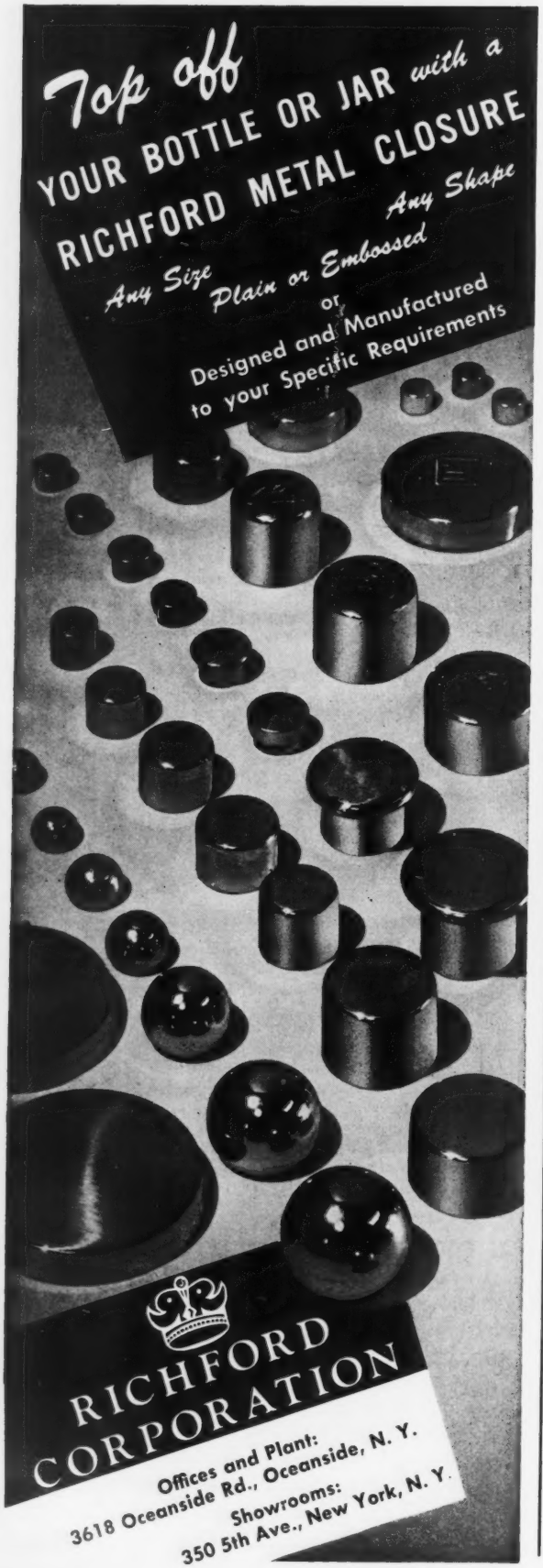


9:1 (see Figure 1, column 3). At the same ratio, the 50 per cent solution shows slight opalescence and is rated between opalescent and clear. Both of these solutions are attractive in appearance and cosmetically desirable.

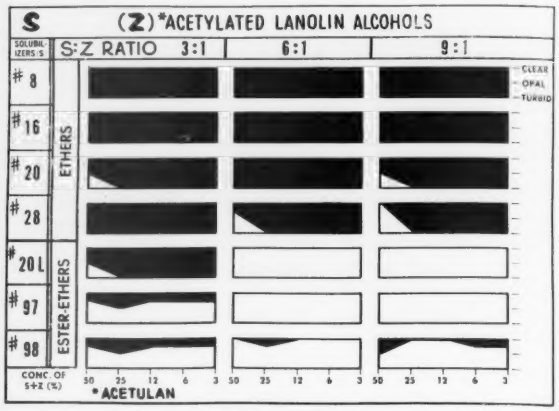


Figure 4

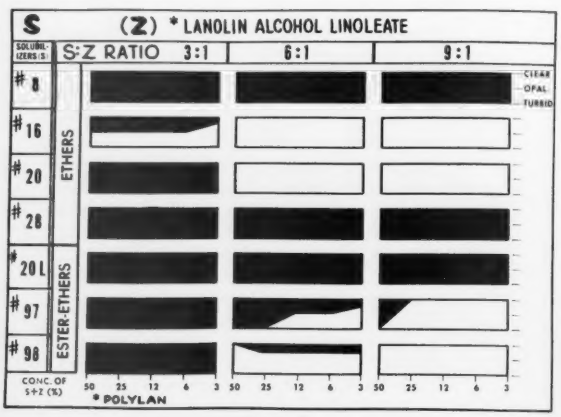


Figure 5

Solubilization of Lanolin

The best result in solubilizing lanolin was obtained with the ether formed by lanolin alcohols and 16 mols E.O. Both 6:1 and 9:1 S:Z ratios produced clear solutions over the complete range of concentrations. At a ratio of 3:1, opalescent solutions were obtained only at certain concentrations. When the chain length was increased from 16 to 20 mols E.O. good solubilization of lanolin was still obtained at a ratio of 9:1. Loss in solubilizing power resulted not only from lengthening the E.O. chain to 28, but also from decreasing its length to 8 units. It appears that the optimum for this group is at 16 mols of E.O.

Among the ester-ethers, the acetylated products #97 and #98 gave best results, forming clear solutions at 9:1 ratio and opalescent solutions in several concentrations at the 6:1 ratio. #20L which was not acetylated, showed only slight activity.

Liquid Lanolin

Solubilizers of both ether and ester-ether types suc-

cessfully solubilized liquid lanolin. The most effective solubilizer was again the 16 mol E.O. adduct. This solubilizer was active over the three ratios and at all concentrations. Good solubilizing power was also demonstrated by the 20 mol E.O. ether. The three ester-ether adducts also evidence activity, the acetylated solubilizers being most effective.

Acetylated Lanolin

It is aparent from the data that acetylated lanolin is relatively difficult to solubilize except in a few instances. Among the ethers, the 16 mol E.O. adduct was the only effective one. It resulted in clear solutions at 6:1 and 9:1 ratios over the full range of concentrations. As for the ester-ether solubilizers, #97 and #98 were effective at 9:1 ratio, while #20L showed no activity.

Acetylated Lanolin Alcohols

The acetylated lanolin alcohols were readily solubilized by the ester-ethers. The 6:1 and 9:1 ratios resulted in clear solutions at almost every concentration with all three of these solubilizers. The 3:1 ratio yielded opalescent solutions with #97 and #98.

The ether type solubilizers were almost completely inactive in this case although these same solubilizers were consistently effective in solubilizing the other lanolin materials.

Lanolin Alcohol Linoleate

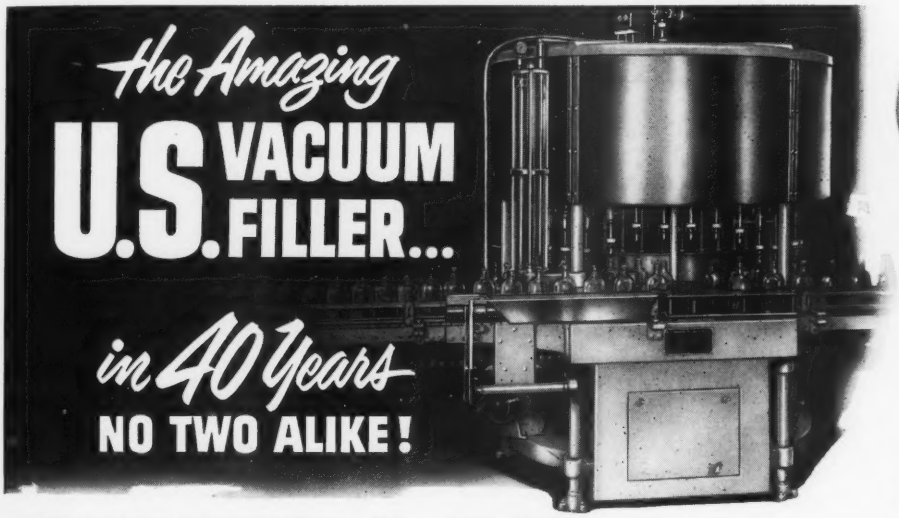
This ester of an essential unsaturated faty acid was readily solubilized by both ether and ester-ether type solubilizers. Again, as in the previous cases, ether adducts containing 8 and 28 mols of E.O. were ineffective solubilizers, while the 16 mol adduct was the most effective. Solubilization was also achieved by the acetylated ester-ethers, #97 and #98, while #20L was ineffective.

Additional Application Studies

Additional experiments were carried out employing all the lanolin-derived solubilizers with the exception of the 8 mol adduct which was previously found ineffective. These were used in combination with typical water-insoluble cosmetic materials as solubilizates (Table V).

All of these materials were successfully solubilized at useful concentrations in aqueous solutions. The technique of stepwise dilution was employed as described in previous experiments, except that the dilution of the S/Z mixture was adjusted to yield the final concentration of Z indicated in Figure 6 (p. 238). The concentrations chosen were practical ones such as would be used in the preparations of consumer products based on the solubilization phenomenon. The appearance of each final concentration was rated clear, opalescent or turbid.

In the case of hexachlorophene a quantity of pro-



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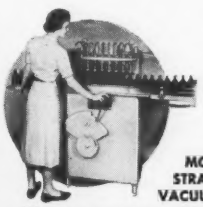

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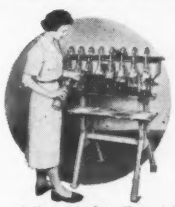

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pylene glycol equivalent to twice the weight of the S/Z mixture was added, imparting a cosolvent effect which was required in this case for solubilization. Similarly, solubilization of Vancide 89-RE was greatly enhanced by cosolvency in acetylated lanolin alcohols. Control experiments omitting these cosolvents did not achieve successful solubilization.

On the basis of the data in Figure 6, the ether solubilizers #16 and #20 were the most versatile in their ability to solubilize the diverse raw materials of this series. All three ester-ether solubilizers demonstrated appreciable levels of activity. As expected, the higher S:Z ratios were superior when more than one ratio was used. However, the 3:1 ratio proved to be adequate for the perfume and the extract of lanolin alcohols with most of the solubilizers. This indicates the advisability of including low S:Z ratios in experimental solubilization studies.

(Z) SOLUBILIZATES	% FINAL CONC. (Z)	RATIO S:Z	(S) SOLUBILIZERS					
			ETHERS			ESTER-ETHERS		
			#16	#20	#28	#20L	#97	#98
PERFUME	.25	3:1	C	C	T	C	T	O
PERFUME	.25	6:1	C	C	C	C	C	C
VANCIDE 89 RE	.04	6:1	T	T	T	C	O	O
MINERAL OIL	2.0	3:1	T	O	T	T	T	T
MINERAL OIL	2.0	6:1	C	O	T	C	T	T
HEXACHLOROPHENE	0.5	6:1	C	C	C	T	T	T
VIT. A PALM.	0.2	3:1	O	T	T	T	T	T
VIT. A PALM.	0.2	6:1	C	C	O	T	O	C
VIT. A PALM.	0.2	9:1	C	C	O	O	C	C
EXT. LAN. ALC.	2.0	3:1	C	O	T	T	O	O
EXT. LAN. ALC.	2.0	6:1	C	C	T	C	C	O

LEGEND: C=CLEAR O=OPALESCENT T= TURBID

Figure 6

It is interesting to note that Vancide 89-RE and Hexaclorophene, were successfully solubilized. Although it is well known that non-ionic ethylene oxide derivatives have an inhibitory effect on the action of antiseptics, preliminary studies have indicated considerable retention of activity in the presence of these lanolin-derived solubilizers. (This is the subject of another investigation which is still in progress.)

Observations of the solubilized perfumes indicated good fragrance characteristics. While the vitamin solubilizations may prove to be of interest, oral toxicity and vitamin assays have yet to be completed. As in the first series, many of the 50 per cent aqueous solutions of the materials in Table V were clear stiff gels, offering interesting product possibilities in cosmetic sticks, hair grooms and moisturizing preparations.

Discussion

It is well to consider at this point the several factors which were found to influence solubilization. It is obvious from the data presented that the higher S:Z ratios give consistently good results. It is equally apparent that good solubilization may be achieved in other instances at lower ratios. Cosolvents such as propylene glycol and ethanol, help reduce the S:Z ratio to a low level. Solubilized perfume solutions may be prepared with as little as 1:1 ratios when alcohol is added. In preparing the 50 per cent concentration of an S/Z mixture, it is important to heat to an optimum temperature for proper solubilization. This heating requirement is best determined empirically for each system under study. Rapid cooling of the heated dilutions often improves the degree of clarity since by this technique opalescent gels or solutions may be converted to a clear system.

Although each system cited in this study contains but one solubilizate, excellent effects can be obtained by solubilizing combinations of materials. For example, perfectly clear gels containing both lanolin and mineral oil have been prepared (4).

The possibilities offered by solubilization with lanolin derivatives are truly unlimited. Conventional water-insoluble emollient materials may be considered in the light of their aqueous solutions, fortified emollient-wise by the lanolin radical of the solubilizer. The conditioning effects of occlusive substances are currently the subject of considerable study with relation to the ever-present problems of skin emolliency. The role of solubilized aqueous systems of thes substances certainly merits investigation in this regard. As previously mentioned, it is possible to prepare emulsions in which oil-soluble active constituents are incorporated in both the oil and water phases. This novel way of introducing materials into both phases of emulsions, with the strong possibility of enhanced active ingredient effects, should be of great interest to investigators in the cosmetic and pharmaceutical fields.

The lanolin-derived solubilizers discussed herein are valuable cosmetic materials from several viewpoints. They offer many formulating advantages due to their good solubility characteristics in aqueous and alcoholic systems and their gelling and viscosity-building properties. The emollient after-feel which they impart to skin and hair, as well as the conditioning effects obtained, are additional advantages gained from these solubilizers.

Summary

A series of lanolin-derived solubilizers has been prepared and investigated for solubilization activity. These products are ethylene oxide adducts of the ether and ester-ether types. A technique for solubilization is described and the importance of a systematic empirical approach stressed. The most effective solubilizers are the 16 mol ethylene oxide ether and the acetylated ester-ethers containing 9 to 11 mols of ethylene oxide. These lanolin-derived products are excellent solubilizers for water-insoluble lanolin materials such as acetylated lanolin, acetylated lanolin alcohols, liquid lanolin, lanolin alcohol linoleate and lanolin itself. The systems solubilized have an unusually high emollient level since both solubilizer and solubilizate are emollients in their own right. These

products are also of great value as solubilizers for a host of other water-insoluble materials. Examples of solubilized products which are potentially useful in cosmetic and pharamaceutical formulations are given.

This study has demonstrated that lanolin-derived solubilizers are important new tools in the hands of the cosmetic and pharmaceutical chemist for the development of valuable new consumer products.

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2—Griffin, W. C., **J. Soc. Cosm. Chem., 1**:311, 1949.
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BIOLOGICALS

(Continued from page 165)

to clarify and improve the regulations and see to it that they adequately set forth standards designed to assure continued safety, purity and potency of all products. No effort is being made, however, that might disrupt the good relationship we have enjoyed with the industry for so many years and which we are confident has accounted for the success attained in providing safe, pure and potent products for the public.

Finally, you no doubt have an interest as to the relationship between the biologics control provisions of the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act. Both contain provisions that neither is to affect or impliedly modify or supersede the other. Clearly a biological is a drug subject to the Food and Drug Act and thus subject to the provisions regarding misbranding and adulteration whether or not the product is licensed under the Public Health Service Act. By regulation, if a biological is a "new drug" and is licensed by the Secretary under the Public Health Service Act, an effective new drug application is not required under the Federal Food, Drug, and Cosmetic Act. On the other hand, if a biological is not so licensed, there is little to be gained by filing a new drug application since commercial interstate shipments would still be unlawful under the Public Health Service Act. The continuation of both statutes by Congress for so many years reflects, we believe, a continuing assumption that controls over and beyond those applicable to drugs generally are required for biologicals. Thus what might be termed "dual" requirements as to biologicals is not unlike "dual" requirements under the Federal Food, Drug, and Cosmetic Act itself where, for example, insulin and certain antibiotics are subject to batch testing even though they are also subject, with certain exceptions, to the general provisions of the Act relating to adulteration and misbranding.

To further contrast these laws or extend this discussion to contrast the subject provisions of the Public Health Service Act with any other Federal regula-

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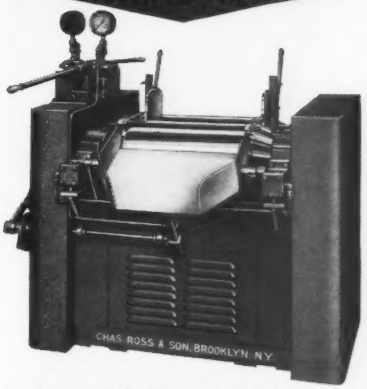

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tory statute would be to seek your indulgence far beyond my reasonable dessert. I believe it is sufficient to say that the provisions of the Public Health Service Act for the regulation of biological products for the prevention, treatment, or cure of diseases in man are sound; that they have been so well accepted by those to whom they apply and so well administered by those charged with that responsibility as to occupy a special position among all Federal regulatory measures. To me this is a great compliment to all of those who through the years have carried out and followed its provisions. They have had one purpose, one common goal, namely, to protect the public health. They have indeed rendered valuable public service.

AFRICAN RARITIES

(*Continued from page 167*)

very fragrant flowers. The popowia cape gives a yield by steam distillation of an essential oil of the patchouly type, but greener and more spicy in odor character.

Kara-karounde or karo-karounde, is another West African perfume plant. Its botanical name is leptoctinia senegambica, of the N.O. rubiaceae, from which family we will know e.g. the gardenia. The natives call it kaulathi or fara-koronte, etc. Considering the fact that there are hundreds of West African plants which might be of perfumery interest, it is a little surprising to see this plant being used, and hardly any of the others. One reason could be, that this plant is fortunate enough to grow in the Fouta-Djalon district of French Guinea, where large French perfume houses have quite modern installations, and are able to produce flower extracts on the spot. The C.A.P.P. (Compagnie Africaine des Plantes a Parfums) has extensive plantations of lemon, bitter and sweet orange, jasmin and a few other perfume plants in the beautiful, mountainous Fouta-Djalon region. The main centers ot production are Mamou, 200 miles east of the seaport Conakry, and Labe, about 100 miles north of Mamou, both at approximately 3,000 to 5,000 feet altitude. There is an inland railroad from the seaport Conakry passing by Mamou, and a motorable track from Mamou to Labe.

The large, white flowers of the karo-karounde are extracted locally with petroleum ether, and the concrete, which comes in a very poor yield, is exported to France for further processing. The yield of absolute from the concrete is, however, very good. My original samples were thus only concretes, but these were in themselves some surprising perfume material.

I had met the shrub occasionally in the French Sudan when I rumbled along the desertous tracks on my lonely motor trips, but these plants were probably botanical variations of the true karo-karounde which is, to my knowledge, only exploited in French Guinea. The very dark, waxy concrete has a strong, not immediately pleasant odor. The material is charac-

terized by its high content of phenylacetonitrile, also called benzyl cyanide. It is one of the few flower products to contain a nitrile at all. But as the odor of phenylacetonitrile is not unlike that of benzylformate (note also the structural similarity!), the karo-karounde absolute can be justly classified among the jasmin-type perfume materials. It is tempting to draw conclusions, but let us content ourselves with remembering that the main constituent of gardenia absolute (a botanical cousin to the karo-karounde), is benzylacetate, which is surprisingly rare in nature. Like longoza-concrete, mentioned below, the concrete of karo-karounde is also remarkable for a vanilla- or chocolate-like odor, although combined with a somewhat nauseating fruitiness. Used with utmost care and discretion, this perfume material can certainly impart unusual notes to fine perfumes. The annual production of karo-karounde concrete is at the level of 100 lbs.

AMBRETTE SEED OIL: During my stay in Nossi-Be, the tiny perfume island off the northwest coast of Madagascar, I had the pleasure of meeting quite a number of "rare" perfume plants. Ambrette seed was produced in the island, but was not distilled nor extracted on the spot, although installations are at hand. A minor export of the seeds to French perfume houses revealed however, that this material is still in demand. For some odd reason, ambrette seed seems to have been forced out of business, out of the everyday life of the perfumers. I realize that the most recent prices are not at all attractive, but this is actually a result of the fact that the seed is not produced on a large scale. When interest fails, the growers will rapidly switch over to other cultivations, and we cannot blame them. I know, however, a very hard working and enterprising perfume plant grower in Angola, Portuguese West Africa, who has laid quite a substantial area out for the cultivation of hibiscus abelmoscus.

The plant is 2½ to 4 feet high, and the fruits, capsules, produce a wealth of tiny seeds. When fully mature, the seeds have a faint musky odor. Immature, they are odorless. The seeds are dark-brown, about 0.12 inch in diameter, and slightly kidney-shaped. The outer tissues, epidermis, contain numerous oil cells in fine rows, the cells "protected" by a layer of palmitic acid, probably exuded from the germ. Contrary to what has been reported in well-known works on essential oil production, it is not necessary to crush the seeds before distillation. In fact, if the seeds are crushed, the germ tissue will yield a large amount of palmitic acid, and the resulting product will be a concrete, containing about 20 per cent of odorous, essential oil. A troublesome removal of the palmitic acid is then necessary. The seeds can be extracted directly with various hydrocarbons etc. to produce concretes and absolutes, according to the solvent in use. Steam distillation of the whole seeds yield 0.3 to 0.4 per cent of a yellowish, liquid oil of a fatty, rather unpleasant

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odor, occasionally with a touch of furfural-note (from the epidermis). On aging, even after a few months, the furfural note disappears, and a beautiful flowery, and incredibly persistent, musky fragrance develops.

One of the interesting constituents of ambrette seed oil is farnesol, sesquiterpene alcohol of faint, but very persistent, flowery odor. Another is the small, but highly effective amount of cyclohexadecenolactone, better known as ambrettolide. This material belongs to the few, so-called animal perfume materials occurring in plants. No doubt an interest from the perfumers' side, resulting in an increased demand, could easily make this beautiful perfume material a more commonly available one, and bring down its price to a level where synthetic ambrettolide and farnesol would no longer be a threat. Most ambrette seed oil is produced in Europe and U.S.A. from imported seed grown in the Seychelle islands, Nossi-Be, Angola, East India or Equador. Ambrettolide is snythesized in several European factories, but cannot be considered as a replacement for ambrette seed oil. This is just as true as vanillin is no replacement for vanilla bean extract.

Also in Nossi-Be, I found champaca, a large tree of the N.O. magnoliaceae. Its brilliant yellow flowers were extracted on the spot by S.P.P.M., the French perfume house, which has adequate extraction installations on the island. The flowers exhale a most beautiful fragrance, at the same time reminding one of ylang-ylang and jasmin, but with a peculiar, dry flower-note similar to that of a good quality of tea. The S.P.P.M. produced annually about 50 to 100 lbs. of a concrete by petroleum ether extraction. Benzene extraction had also been tried. This quantity of concrete demanded some 3 tons of flowers (5 or 6 tons per 100 lbs. concrete), and the harvesting of flowers from the tall, slender trees is not at all easy. It is not possible to increase production rapidly because of the slow growth of these trees. Harvesting in Reunion island has ceased, but during my recent visit, I could still find many trees in full bloom. Extraction installations, originally brought to Reunion by Garnier in 1910, has been transferred to Nossi-Be and the Comores.

The champaca-concrete from Nossi-Be is shipped to France, where it is processed into an absolute. The yield is about 50 per cent. The materials responsible for the odor are mainly esters, and also about 3 per cent isoeugenol. A few French perfume houses profit from the almost monopolized use of the exquisite perfume material, and among the commercially available, so-called champaca-absolutes, there are several, which are nothing but ylang-ylang with "bouquetting" notes. The Philippines, Indonesia and India produce small quantities of champaca, but often cut the product with ylang-ylang or cananga, usually by co-distillation of the two or three sorts of flowers. Hence the apparent lack of interest in commercial Champaca. If the customers only always received the true

champaca, they would certainly have asked for more than the first sample. In Nossi-Be, although this island produces substantial quantities of ylang-ylang, I could assure myself, and thereby the readers, that the champaca produced there is extracted exclusively from champaca flowers. Once you have smelled the true champaca, nobody can fool you with an adulterated one again.

There is still another plant in Nossi-Be, which yields a rare and interesting perfume material. That is Longoza, also called "garland" in English-speaking territories. The botanical name is hedychium flavum. It is a man-high plant. It grows also in Reunion island, whereto it was imported during the 19th century together with champaca and black pepper from the East Indies and Malacca. The flowers of longoza are situated on a separate stem close to the ground and well protected by the long leaves. In some aspects, the plant loks like its much smaller cousin, ginger. The flowers are white or red-and-white, and very fragrant. By petroleum ether extraction, the SPPM in Nossi-Be produces a concrete in a very low yield. The plant grows abundantly, wild and semi-wild, also along the Madagascar East Coast, but is apparently only exploited in Nossi-Be, and only when there is a demand for the concrete. Here again, certain French perfume houses will buy the entire production and process it into an absolute. This, in turn, ends up in high class French perfumes, and, recently, has been introduced as a flavor ingredient in vanilla and chocolate flavors. Thus, longoza belongs to the very few perfumery materials, which possess a chocolate-like flavor. The concrete is a brow mass of honey-like consistency, melting at about body temperature. Its odor reminds one at the same time of chocolate, vanilla and orange flowers, and posesses definitely spicy undernotes, which enable this product to impart quite unique effects in perfumery. The absolute is an extremely powerful material which must be used with utmost care, skill, and experience. An overdose may ruin the perfume just as easily as the correct dose will produce inimitable effects. The entire production of longoza concrete in Nossi-Be is about 50 lbs. per year, but it could easily be increased to several hundreds. All is consumed by France.

The flower, when not harvested, will produce a fruit, which, by the way, is a local delicacy among the children. I tried it myself, and the almond-like, mucous, white fruit was indeed quite tasty and refreshing. Although a little bland, it was slightly spicy and reminded me much of the taste of fresh cocoa seed.

To conclude this very small and concentrated report on some "rare" and "hard-to-get" perfume oils, I would like to draw the attention of pandanus. I had met this small tree quite often in Reunion island and Madagascar where it is used as a supporting stem for the vanilla vines, and occasionally in Africa as a decorative plant. In several aspects this plant is highly

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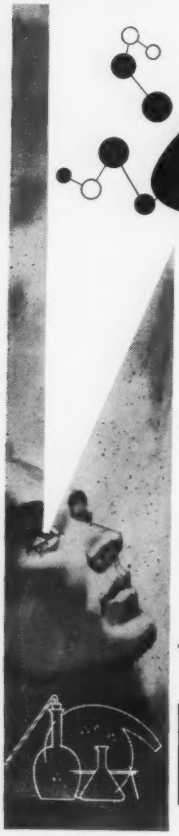

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interesting. The most impressive is probably the flowers. They are cream-colored, almost white, and if you pick three you may have your first lb. of flower material for the perfume extraction. One drawback is, however. that there are seldom more than 15 or 20 flowers (about 5 lbs.) on each tree. To my knowledge, the flowers are not exploited for perfume production in any of the above mentioned places, but in India, between 100 and 200 tons of flowers are treated yearly. The Hindu's call the flower "kewda", and it is one ofthe most important perfumery materials in India, as far as odor type is concerned. The flowers fill the air around the trees with a heavy, sweet, yet very hyacinth-green fragrance, but I am not able to tell much about the odor of the perfume oil. The samples, I have received years ago, were probably the common Indian sandalwood-cedarwood, distilled over pandanus flowers, or the like. Experimentally distilled oils, steam-distilled in India, show the following approximate composition (according to "Schimmel's Miltitzer Berichte"): 65.97 per cent methylphenylethylether, 18.71 per cent d-Linalool, 3.48 per cent phenylethylacetat, 1.82 per cent citral, 8.31 per cent dipentene, 0.49 per cent acids, calculated as caproic acid, traces of P.E.A. and other components. A glance at the chemical constitution of the major component shows a definite relation to the phenylacetic aldehyde type of perfume materials. The yield of essential oil by steam distillation is about 0.03 per cent, and it is an advantage to lead the mixed vapors into petroleum ether to insure a good separation of the oil-phase from the distillation water. An absolute can be produced from the benzene extraction concrete (0.13 per cent of the flower material) by subsequent alcohol extraction (25 per cent of the concrete). The oil is not commercially available, probaly due to the fact that the entire Indian production of flowers is processed to a perfumed oil by a very old maceration method, not unlike the French "enfleurage" or the "pomade" method. A perfumed water is also produced and is very popular. A few Hindustani perfume factories may produce absolutes or similar extraction products for local consumption.

Pandanus also grows on the various island groups in the Indian Ocean and in certain areas of southern Arabia and Iran. But to mention only the unexploited fragrant plants which I met on my transAfrican trips, would fill pages with dry notes of insignificant botanical names and poor attempts to describe odors which we cannot carry home in a bottle—yet.

So, while Mother Nature every years wastes thousands of tons of perfume where often no human being can enjoy it (and, to be justly, the perfume was not meant for us!), other people are extremely busy producing new, synthetic, odorous materials at a rate, which might even impress Mother Nature. But I doubt, whether our synthetic perfumery materials generally impress her. The absolute fact is, however, that synthetic perfumery materials make out an in-

creasing percentage of the total world production of perfumes for all sorts of cosmetics,—and that these products are appreciated by the customers. Man's customers, not Mother Nature's. *Very* few of the *very* successful synthetic perfumery raw materials are *not* found in Nature.

HORNY LAYERS

(*Continued from page 170*)

imum extractable amounts, as much as any of the dispersants (Table VII). In these experiments amino nitrogen was estimated with ninhydrin (7).

TABLE VI

—SH in mMx 10^{-3}/100 Gm. dry weight tissue in psoriatic scales.

Incubated with:	
Water	16
Allantoin (0.2%)	60
Urea (10%)	66
Aluminum chlorhydroxy allantoinate (0.2%)	30
Duponol (10%)	98

TABLE VII

Free alpha amino nitrogen in mg/100 Gm. dry weight in pulverized scales after extraction with various agents.

Extracting fluid	Exfoliative dermatitis	Type of scale Ichthyosiform erythroderma	Psoriasis
None	—	—	85
Water	71	51	80
Urea (10%)	73	62	85
Allantoin (0.2%)	75	50	85
Aluminum chlorhydroxy allantoinate (0.2%)	69	54	78

Discussion

Although much has been written about "dry skin," "chapped skin" and "scaly skin," the essential features of these conditions have not always been clearly described. There are at least two anomalies in such skin surfaces: 1. Dryness, that is lessened water-holding ability and 2. the formation of adherent scales which are the result of insufficient break-up of the horny layer. Lacking a better term, we will refer to this anomaly as "stickiness," which means that the horny cells adhere to each other and to the underlying cellular layers.

1—The dryness is the outcome of a defect in the water-binding components of the horny layer. These components are in the soluble fraction of the stratum corneum and, after pretreatment with lipid solvents, can be extracted with water. Thus dryness may be produced artificially by treating the surface with lipid-solvents and water or with detergents. Under some pathologic conditions the quantity, quality, or both of these components may become abnormal; these pathologic horny layers hold abnormally little water. The lessened water-binding resides in the water-soluble fraction of the horny layer; both the rate and extent of the water-uptaking ability of this fraction are seriously impaired (8).

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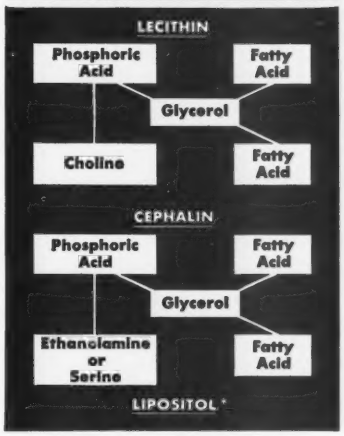

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The chemical nature of the hygroscopic components of the skin surface is still unknown. In all likelihood, the water-binding ability is in some way related to the free alpha amino nitrogen content of the scales. In our studies all horny layers with a low water-binding ability had a low free alpha amino nitrogen content, while normal hygroscopicity was associated with the high alpha amino nitrogen content of normal horny layers. The recent suggestion by Szakall (9) that at least a part of the water-holding capacity of the horny layer is due to a combination between pentoses and amino acids, requires further confirmation.

2—The stickiness of the horny layer leads to the formation of visible scales. Normally the horny layer desquamates in the form of invisible, dry particles (10); presumably the cornified cells fall apart and are cast off individually. Whenever keratinization is accelerated, as after ultraviolet erythema, in psoriasis or exfoliative dermatitis, the horny layers fail to break up, but form more or less extensive white or silvery scales which often stick to the underlying cells. The stickiness is probably due to persistence of an intercellular cementing substance. The chemical nature of this cementing substance is not known, but there is some indication that it may be a mucopolysaccharide. Roe's recent finding of a glycoprotein in extracts of scales from psoriasis and exfoliative dermatitis (11) extend and confirm previous histochemical observations (12). Our recent findings of the occurrence of glucosamine, both free and bound, in extracts of horny scales also point in this direction.

Dryness and stickiness are often associated, but may occur independently, as in ichthyosis vulgaris or keratoderma plantare, where the scales are sticky, but bind normal amounts of water.

When we try to break up the cohesive horny layer with dispersing agents, we attempt to remove or dissolve the intercellular cementing matrix, without attacking the epidermal cells. This task is not easy. Lithium bromide, the best dispersing compound in our study, is extremely irritating in the recommended concentrations. Its use is solely of academic interest and attempts to introduce it clinically have not gained acceptance (13). Urea is of value in conditions with thick horny accumulations; it has a "drying" effect in the high concentrations it has to be used. Even salicylic acid, the most common "keratolytic" agent, will sometimes attack the epidermis ("retecytolysis") and is of limited value in breaking up large coherent scales. Detergents apparently have a double effect. Although they remove water-soluble substances and lipids and probably attack the hypothetical intercellular matrix, they also combine with proteins and thus may form a new "cement." The prolongation of the flow rates in pulverized scales, after extraction with detergents, may be based on such a secondary combination between epidermal proteins and detergents. On the other hand, allantoin, although not as power-

ful as some of the other keratin dispersing agents, cannot be used in hypertonic solutions; at room temperature its concentrated solution is less than O.1M and therefore it does not attack the living epidermal cells. On the basis of results obtained *in vitro* it has been introduced as an adjuvant for the topical treatment on scaling diseases with promising results. Preliminary clinical reports (14) obtained with such preparations show that *in vitro* methods can play an important role in screening and testing compounds before they are presented to the fields of cosmetics or dermatology.

Summary

This study deals with several methods for determining the ability of various chemical agents to disperse the horny layer.

I—In one set of experiments, we measured the rates of flow of various oils through a standardized column of pulverized horny scales. The main findings were as follows:

1—The flow rates depend on the type of oil tested, regardless of the nature of the scales.

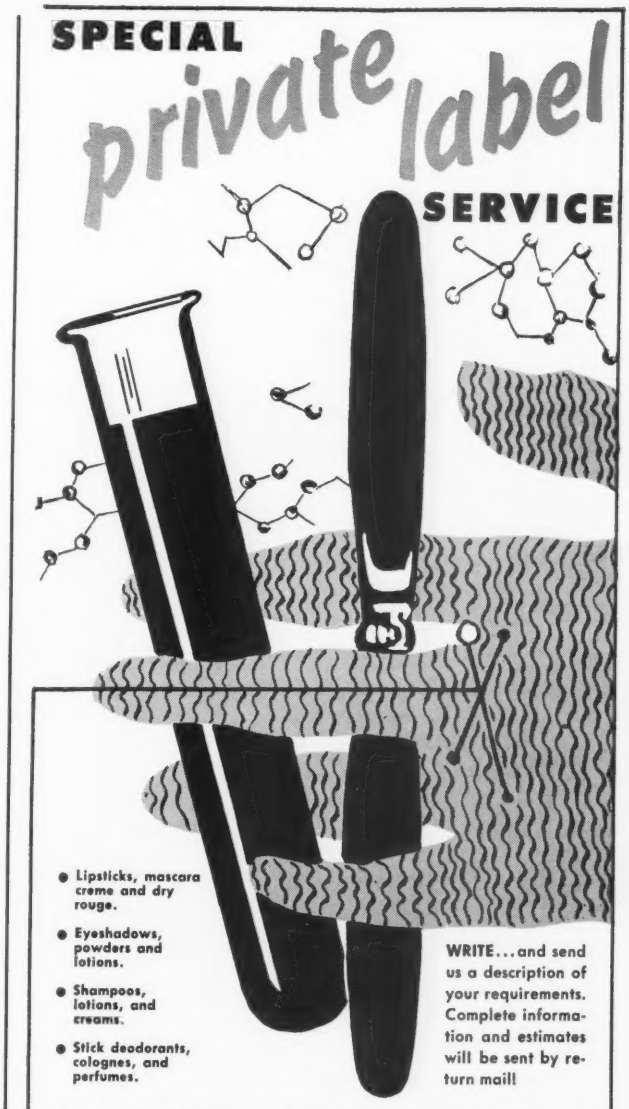
2—Compared with normal specimens, the flow rates through pathologic scales were extremely prolonged.

3—Agents which disperse the horny layer, greatly accelerate the rates of flow. Among these agents we tested 75 per cent lithium bromide, 10 per cent urea, 0.2 per cent allantoin, 0.2 per cent aluminum chlorhydroxy allantoinate solutions and detergents. The order of activity was: lithium bromide, allantoin, urea, aluminum chlorhydroxy allantoinate. Detergents generally retarded the flow of oils through the powdered horny layer.

II—Microscopic studies of scales after immersion into water, urea, allantoin and aluminum chlorhydroxy allantoinate also revealed the dispersing ability of these substances.

III—In chemical studies we estimated the amounts of extractable sulfhydryl and free alpha amino groups. With the dispersion of scales, the concentration of the extracted sulfhydryl groups increase. These groups are bound to the soluble proteins in the horny layer and may be estimated after dispersion of the scales. By such a test, the keratin dispersing effect of allantoin was also ascertained. On the other hand, the amounts of extractable free amino groups cannot be used as an index of the desaggregation of the horny layer. Water alone extracts the maximum amounts of these groups and protein dispersants do not increase the quantities of extractable amino nitrogen.

On the basis of the present and previous work the theory is advanced that in "chapped," "dry" and "scaly" skin we deal with two independent features which may or may not appear together: 1. Dryness, which is due to deficiency in the water-soluble hygro-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scopic components of the horny layer: and 2. stickiness, which is probably caused by the persistence of a cementing matrix between the horny cells, resulting in the formation of visible scales which adhere to the skin surface. The nature of the hygroscopic components is unknown; our work indicates that in some way they are related to free amino groups. The hypothetical cementing matrix is equally obscure: some of our recent experiments suggest that *epidermal* mucopolysaccharides may play a role.

The described methods are useful for the testing of new dispersing agents for dermatologic or cosmetic application. On this basis allantoin has been introduced recently as an adjuvant in the topical treatment of psoriasis and of some other scaling skin diseases.

Acknowledgments

The author wishes to express his thanks to Chesebrough-Pond's Inc. and the Schuylkill Chemical Company for their assistance and to Robeco Chemicals, Inc. for supplying chemicals for the test.

From the Department of Dermatology (Donald M. Pillsbury, M.D., Director), University of Pennsylvania School of Medicine. This study was supported in part by a grant from the National Institutes of Health, P.H.S. RG-4718, and by a grant from the Squibb Institute for Medical Research.

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ROUGES

(*Continued from page 163*)

All fats, oils and preservatives are heated to 68° C. For the anhydrous type heat the bromo acid and castor oil together. Premix white and pigments. Blend with other oils and pass through roller mill twice. Reheat and keep at 5° above setting point. Pour into containers; avoiding excess air. The water, emulsifiers, and humectants of the vanishing and emulsion types are heated to 70-72° C. and poured slowly into the oil phase at high speed until homogenous. The speed is then reduced to moderate and mixing continued. While cream is mixing blend the pigments in a pony mixer or ribbon blender and pass through hammer mill 0.013 H. B. Screen. When cream temperature has dropped to 50°C., remove a portion (about 15 per cent) and blend in the pulverized pigment, pass through a roller mill twice and return the ground mass to the batch. Continue mixing till color is completely diffused, add perfume. Pour into compacts at a few degrees above the setting point. To avoid streaking of light shades that contain a high per cent of white extenders, substitute alumi num hydrate for part of the whites.

Rouge Stick

The molded rouge stick is basically a lipstick, modified to a softer texture, for easier application and better diffusion, and containing a small amount of bromo acid.

A typical starting formula might be:

Crystal O castor oil (4)	70.00
Carnauba wax	5.00
White ozokerite	4.00
Beeswax	4.00
Preservative	0.20
Lanolin	3.00
Butyl stearate	3.50
Bromo acid—Red 21 or Orange	0.30
Earth and/or lake pigments	10.00
Perfume	q.s.

Heat the castor oil and butyl stearate to 70° C, add the bromo acid, stir, add the pigments, stir, pass through roller mill twice and set aside hot to dissipate the entrapped air. Melt the waxes, lanolin and preservative, add the milled colors and mix till the entire mass is homogenous. Maintain temperature at 10° above setting point. Pour into preheated aluminum molds, scrape off excess mass, and chill molds before discharging. Reheat and dry the molds before each cycle.

Liquid Rouge

The increasing popularity of liquid rouge is based on the fact that the user will attain the "natural look." A drop or two, applied after a liquid foundation, diffuses well and shows no line of demarcation. The earliest form of liquid rouge consisted of an alkaline solution of carmine, with small amounts of humectant and perfume. The modern version consists of a creamy liquid emulsion containing water-soluble certified colors, and/or pigments; or, a suspension of pigments in the presence of colloid agents and humectants.

Typical experimental formulas might be:

LIQUID ROUGE

	a	b	c
CMC or polyvinyl alcohol	2.00	—	—
Triton X 100 (6)	0.25	—	—
Water soluble Red (FDC red 3)	0.50	0.50	—
Propylene glycol	2.50	1.60	10.00
Lanogel 41 (7)	1.00	1.50	0.50
Water	93.55	87.50	—
Cetyl alcohol	—	0.50	—
Glyceryl monostearate	—	7.50	—
Duponol ST (8)	—	0.40	—
Methyl p-hydroxybenzoate	0.20	0.20	0.20
Absorption base	—	—	5.00
Isopropyl myristate	—	—	15.00
Span 60 (3)	—	—	0.50
CMC gum 70—High (9)	—	—	0.15
Zinc oxide	—	—	4.00
Titanium dioxide	—	—	8.35
Albatex (5)	—	—	4.30
Tween 60 (3)	—	—	2.00
2% Veegum slurry (10)	—	—	48.00
D & C Red or Orange Lake	—	—	2.00
Perfume	q.s.	q.s.	q.s.

In formula (a) the water is heated to 80° C., the

preservative and w.s. color added, stir, add the Lanogel 41, stir till dissolved, add the wetting agent and humectant. Finally sift in the CMC or polyvinyl alcohol slowly to avoid clotting. Use a high speed mixer to disperse colloids. Allow to stand overnight before packaging.

In formula (b) the glyceryl monostearate, cetyl alcohol, Lanogel and preservative are heated together to 65° C. in a stainless kettle equipped with a variable speed mixer. The water soluble colors, propylene glycol and duponol ST are heated to 70-72° C. The oil phase is then added to the water phase with rapid agitation till the temperature drops to 50° C., then reduce speed to avoid inclusion of excessive air. Perfume at 40° C. and continue mixing till cold.

In formula (c) the pigments and white extenders are first mixed in a horizontal blender for one-half hour, then passed twice through a hammer mill equipped with a 0.013 h.b. slot screen. Set aside for future use. Heat the fats, oils and preservative 65° C. Heat the Veegum slurry (prepared in advance), propylene glycol and Tween 60 to 70° C., in a stainless steel kettle equipped with a variable speed stirrer. Add the previously milled pigments and the dry CMC to the oil phase and disperse with rapid agitation. Pour the pigmented oil phase into the water phase, with rapid agitation. Wash down the oil kettle with small portions of the newly formed emulsion and combine washings into the emulsion. Continue rapid agitation till temperature drops to 45° C., add perfume, continue to mix at slow speed till the emulsion is cold. Allow to stand overnight to exclude entrapped air before packaging.

All formulas are experimental starting points and must be adjusted to suit individual needs.

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KANAMYCIN

(*Continued from page 229*)

acid fast organisms.

Seventeen patients with moderately or far advanced active chronic pulmonary tuberculosis, with prolonged previous chemotherapy, and with organisms presumably resistant to the major drugs were treated by J. H. McClement et al. with kanamycin 0.5 to 1.5 gm. intramuscularly daily for 2½ to 4½ months.

Eosinophilia of varying degree was noted in 9 patients. No consistent changes in liver function were seen. Granular casts, which appeared 3 to 54 days after onset of therapy, were found consistently in all cases. Transient slight albuminuria was seen in 6 patients, and a few leucocytes in the spun sediment

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were observed transiently in nearly all cases. Isolated and transient elevation of the blood urea nitrogen to 20-30 mg. per cent was observed in 7 cases. Audiometry revealed slight to moderate loss in high frequencies in nearly all patients tested.

Progressive tuberculosis with clinical and radiographic deterioration was seen in one patient. Disease in the remaining patients either improved or showed no change. Slight to moderate radiographic clearing was noted in 4 cases.

These observations reveal no serious toxicity of Kanamycin for humans and suggest some degree of antituberculosis effect of the drug.

Kanamycin was administered intramuscularly at a dosage of 1-3 gm. twice a week; sometimes 1-1.5 gm. is parenterally administered every day or every other day. PAS was simultaneously administered at a daily dosage of 8-10 gm. for all cases, according to a report by I. Donomae.

The results of 79 cases observed over a period of 2-6 months reveal that 64 per cent show sputum conversion on smear, 62 per cent show improved x-ray findings of various degrees, and 54 per cent show a closure or reduction of the cavity. The majority of cases demonstrate clinical improvements such as a decrease in fever, good appetite, weight gain, normal E.S.R., decrease in cough and sputum.

Common side effects of Kanamycin consist of tinnitus, disturbances mostly of high frequency hearing on audiometric examination and eosinophilia. There seldom appear dizziness, skin rashes, headache and paresthesia. No marked abnormalities are found of urine, serum proteins, serum minerals, renal or hepatic functions.

The incidence of untoward reactions is related to individual doses administered, e.g., audiometric disturbances develop in 26 per cent of those who have been administered over 6 g weekly, while they appear only in 2 per cent of those with less dosage.

L. B. Berman and S. Katz reported indications of nephrotoxicity following the use of kanamycin in pneumonia. The clinical course was that of an acute, severely toxic illness, chest X rays and bronchoscopy were consistent with an unresolved pneumonia, right upper lobe. Hemolytic micrococcus pyogenes, var. albus, was recovered from sputum and bronchial washings. A variety of antibiotics, including tetracycline, chloramphenicol, novobiocin, streptomycin and isoniazid, failed to influence the course of the disease.

Kanamycin, 0.5 gm. intramuscularly every eight hours, was begun on 1/31/58. The response to treatment was excellent until 2/13/58 when patient experienced a rise in temperature, delirium, and oliguria. The kanamycin was discontinued after a total dose of 21 gm. Urine output was 15 ml. on the following day and rose over the next three days to 1650 ml. The highest blood urea nitrogen was 75 mg./100 ml., which gradually declined to 30.

A percutaneous kidney biopsy was performed on 3/10/58. It revealed acute tubular necrosis, focal chronic pyelonephritis and arteriolar nephrosclerosis. Endogenous creatinine clearances at this time were 50 ml./1.73 square meters. Patient was discharged with some mild residual atalectasis, right upper lobe.

T. C. Chalmers et al. concluded that kanamycin in doses of 4 gm. or more of the base per day has a definitely beneficial effect on the clinical and electroencephalographic signs of liver failure.

Preliminary studies by W. W. Faloon and C. J. Fisher suggest that oral kanamycin has a profound effect upon fecal flora. The variation in blood ammonia concentrations observed in some patients despite these bacterial changes may be attributable to the presence of bacteroides.

Although the broad spectrum antibiotics, employed systemically, have reduced morbidity and mortality associated with peritonitis and peritoneal contamination, uncontrolled infection still results in a small percentage of fatalities. The intraperitoneal instillation of appropriate antibiotics at surgery affords, a technique for combatting bacterial invasion in these emergency situations.

In a series of 24 patients, ranging in age from 2 to 70 years, intraperitoneal instillation of kanamycin was employed by A. Prigot et al. There were 9 cases of established peritonitis and 15 cases of peritoneal contamination at the time of operation. When surgical intervention was decided upon, a broad spectrum antibiotic was administered intravenously. At the end of the operation, 0.5 gm. of kanamycin, diluted with 20 cc. of sterile distilled water, was introduced into the peritoneal cavity just before closure. Strains of *Esherichia coli*, *Proteus sp.*, *enterococcus*, *Staphylococcus aureus*, *alpha hemolytic Streptococcus*, and *beta hemolytic Streptococcus* were cultured from peritoneal fluid recovered in cases of established peritonitis.

Uncomplicated recovery pertained for these patients except for one case of a 63-year-old patient subjected to subtotal gastrectomy for peptic ulcer.

Kanamycin employed intraperitoneally in conjunction with broad spectrum antibiotics is a valuable adjunct in the surgical management of established peritonitis and peritoneal contamination.

Kanamycin has been administered orally by I. Colin, Jr. to hospitalized patients to evaluate its effect on the flora of the stool as part of a comparative study of various agents for preoperative preparation of the bowel.

In the majority of patients there was control of streptococci, coliform organisms, and clostridia. Staphylococci were controlled in those patients in whom they appeared. Bacteroides were controlled in about half the patients studied. Yeasts proliferated during therapy in about half the patients. No significant numbers of other organisms were found.

There were no disturbing gastrointestinal side reac-

tions. Diarrhea was not produced by the drug. There were no significant changes in sensitivity of the organisms recovered. There was no change in prothrombin time.

On the basis of these studies, and by comparisons with other drugs studied in this laboratory, kanamycin is considered one of the best agents yet found for intestinal antisepsis.

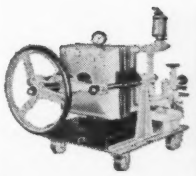
Clinical use of kanamycin by K. J. R. Wightman and P. H. Greey has been limited to patients with stubborn infections due to sensitive organisms which had failed to respond to other antibiotics. These have included two patients with pancytopenia and steroid therapy who responded well in spite of a presumably reduced resistance mechanism. One of these had a serious staphylococcal infection and the other a generalized salmonella infection with positive blood cultures. A group of patients with urinary infections due to aerobacter aerogenes responded well in spite of failure with other antibiotics and in the presence of adverse anatomical features. No toxic effects were noted. The antibiotic is extremely potent although the emergence of resistant strains may prove to be a problem.

Salmonellosis and Bacillary Dysentery remain a constant problem in the practice of pediatrics in the South. These infections have largely been reduced from epidemic proportions, such as they were in the past, to endemic diseases still having a high morbity in infected individuals.

Thirty cases of Shigella infection (*sonnei* and *flexneri*) and thirteen cases of Salmonella infection (B,C,D) were identified and treated by R. V. Platon and W. G. Thurman with kanamycin in a three month period. Several of these cases were quite toxic. Therapy was carried on for five to seven days. The dosage used varied from fifteen to fifty milligrams per kilogram per twenty four hours. The only toxic effects noted were those previously reported relating to kidney function; all of these are reversible after discontinuing therapy.

Results indicate that a dosage range of thirty to fifty milligrams per kilograms per twenty-four hours is safe and is efficacious in the therapy of Salmonella and Shigella infections.

Kanamycin was used by F. R. and A. R. Sanchez to treat 7 cases of anthrax, 2 of typhoid fever, 2 of paratyphoid A and 2 of Brucellosis. It was given by the intramuscular route in doses from 1 to 3 gm. daily for a period varying from 7 to 16 days. Good results were obtained in 6 of the 7 cases of anthrax. In one of the cases of typhoid fever, Kanamycin was associated with phenylbutazone, the latter being given by mouth in doses of 600 mg. daily for 6 days. Results were good in this case, but poor in the other case of typhoid fever. In the 2 cases of paratyphoid A, the results were only fair, as they were in the cases of brucelosis. Tolerance of the drug was good. In some cases, hyaline and granular casts were found in the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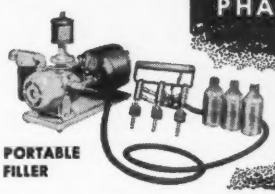
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Kanamycin, a new antibiotic, effective against a range of gram negative bacteria, has been used in the treatment of chronic urinary tract infections in 35 male patients at the Van Duyn Memorial County Hospital by A. H. Dube. The drug was administered 0.5 gm. every 12 hours, intramuscularly, for either a five or eight day course. In 14 patients with pyuria, 12 out of the 14 (86 per cent) had clearing of the pyuria, and 9 of the 14 (64 per cent) had reversal of theirc ultures to normal. The cultural flora usually involved proteus, Aerobacter, alpha strep, and pyocyaneus. Most of the cultural failures involved the pyocyaneous organism. More cultural reversals occurred in those patients receiving the eight-day course of therapy than in those on the five-day program.

In 21 patients who had no pyuria at the time of study but had bacilluria and positive cultures with pyuria at some time in the past, 12 of the 21 (57 per cent) had cultural reversal. Most of the cultural failures again involved the pyocyaneous organism and many in the failure group were on long-term catheter drainage.

Sixteen patients developed hyaline or granular casts during therapy. One week following therapy, the casts had disappeared in 11 of the 16 patients and had diminished in quantity in an additional three of the group. There were no significant N.P.N. or cephalin flocculation changes either during or following therapy.

Kanamycin has been found by A. C. White and V. Knight to be effective *in vitro* against a large number of recently isolated staphylococci of phage group II or phage type 80/81 and other microorganisms which are resistant to many of the presently available antibiotics.

Studies of the adsorption and excretion have shown that levels which are effective *in vitro* can be achieved following intramuscular administration of kanamycin.

No significant toxicity has been encountered in treatment of small number of patients.

R. H. High et al. presented data on serum levels of Kanamycin following its intramuscular injection in a variety of doses. Peak levels are usually reached in one-half to one hour and drop thereafter. Serum concentration of Kanamycin often cannot be detected eight to twelve hours after single doses.

Kanamycin was effective in treating approximately sixty-five infants and children with a variety of infections. Most patients had infections caused by Staphylococcus aureus. The majority of the other infections were caused by gram negative bacilli or Mycobacterium tuberculosis. Kanamycin appeared to be beneficial in most instances and its toxicity was low.

A few observations concerning the use of Kanamycin by aerosolization were mentioned. The drug was well tolerated when used in this fashion.

Eight patients with soft tissue infections and four with urinary tract infections were treated by G. A. Cronk and D. E. Naumann with kanamycin. All patients improved under therapy except one with secondarily infected eczema. There were no recrudescences.

The intramuscular injection of kanamycin was associated with slight burning at the site of injection and was apparently of the same order as the obtained following the injection of saline or penicillin. This discomfort was slightly more intense for 1.0 gram doses than for 0.25 and 0.5 gram doses which may be related to volume (3 ml. versus 1-2 ml.). There were no toxic manifestations following the intramuscular injection of Kanamycin in forty-two humans when administered for a period of from one to six days.

Approximately 75 patients have received parenteral kanamycin for the treatment of various infections; most were caused by staphylococci with small numbers of pneumococcal and various gram-negative bacillary infections according to J. M. Finegold et al. The over-all response to kanamycin therapy was considered good, but there were several clear-cut treatment failures. Most patients were treated with intramuscular injections; local tolerance was fairly good, particularly if procaine or xylocaine were added to the drug. A few patients received the drug intravenously with no untoward effects. The incidence of significant toxic reactions was high, but toxicity was seen primarily in patients who received either large doses of kanamycin, prolonged treatment, or both. The most common manifestations of toxicity were involvement of the VIII nerve (usually only the auditory portion, but sometimes also the vestibular) and renal damage; also encountered were a small number of sensitivity reactions and minor neurological disturbances. Early follow-up studies suggest that the deafness encountered with kanamycin is not necessarily bilateral, complete or permanent. Tinnitus was generally an early sign of auditory nerve damage.

Seven patients received kanamycin orally for intestinal antisepsis or for treatment of Salmonellosis; side effects were generally absent and results were excellent.

To date, development of kanamycin-resistant strains has not been a problem.

Kanamycin was extremely effective in the treatment of patients with infections of the soft tissues, post-operative wounds, urinary tract, respiratory system, and various miscellaneous surgical infections according to A. M. Rutenberg et al. Forty-one of forty-eight patients with infections due to gram-positive and gram-negative bacteria including strains resistant to other antibiotics responded to Kanamycin. Five patients with infections due to strains resistant *in vitro* to the drug failed to respond and in the remaining two results of therapy could not be evaluated because of other measures which could have been responsible for the improvement.

The drug was generally well-tolerated. One pa-

tient showed evidence of ototoxicity and transient impairment of renal function and several others showed hyaline and granular casts in the urine during treatment. No other systemic reactions were encountered.

During the course of a recent staphylococcal outbreak at Jefferson Davis Hospital 36 infants and children were treated with kanamycin by M. D. Yow and G. K. Womack. Seven patients had mild staphylococcal disease, ten were moderately ill, and nineteen were severely ill.

Eighteen of the 36 strains of staphylococci were "epidemic strain 81." Most of the strains were triply resistant to penicillin, streptomycin and the tetracyclines. All strains were sensitive to less than 6.25 mcg./ml. of kanamycin.

The results of kanamycin therapy were uniformly good in the mild and moderately severe cases. Of the severely ill patients, 11 recovered, 1 improved, and 7 died. The causes of failure were felt to be late institution of therapy, extensive tissue destruction prior to therapy, as well as localization of the infection in an area that was inaccessible to adequate surgical drainage.

Side effects of the drug were difficult to assess. It was noted that cylinduria occurred intermittently with dosages above 50 mg./kg./day. However, in no instance was it necessary to discontinue the antibiotic due to toxic symptoms.

During the past six months, 100 patients with resistant bacterial infections have been treated with kanamycin in Houston hospitals by E. M. Yow and O. T. Monzon. Thirty-seven of these were part of a staphylococcal epidemic among newborn infants. Twenty-five of the remaining 63 patients had staphylococcal infections, 11 had infections due to *E. Coli*, 6 had proteus infections, 12 had mixed infections, and there were 9 miscellaneous infections treated.

Of the 63 patients treated, 27 had an obvious beneficial effect from kanamycin therapy; an additional 14 patients were considered to be helped by kanamycin plus some other antibiotic or surgical drainage. There were 10 deaths among the patients treated. One patient died of sever staphylococcal sepsis and four died of pseudomonas septicemia. The remaining five patients died of unrelated causes or because therapy was begun too late in the course of their illness. Kanamycin therapy was considered a failure in 5 additional patients, 2 of whom had severe staphyloccal endocarditis or endarteritis, 2 had deep abscesses without adequate surgical drainage, and 1 had extensive burns with mixed infection.

The dosage used in adults varied from 1 to 3 gm. intramuscularly daily. The smaller dose may have contributed to the failure in some instances.

There were no significant undesirable side effects except for diminution in auditory acuity in one patient.

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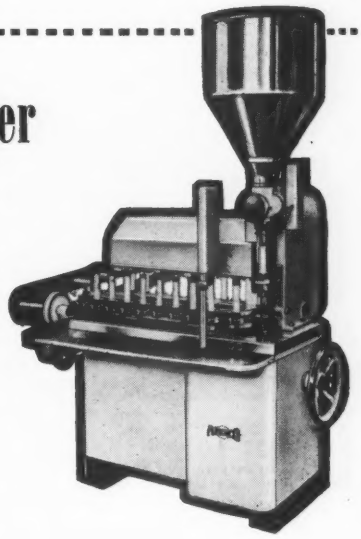

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ADVERTISING INDEX

Aceto Chemical Co., Inc. 226
American Cyanamid Co. ....Facing 138
Anchor Hocking Glass Co. 186-187
Ansbacher-Siegle Corp. 246
Arenco Machine Co. 253
Aromatic Products, Inc. 200
Atlas Powder Co. 144-145

Barr & Co., G. 176
Beauty Fashion 146
Bernardin Bottle Cap Co. ....Facing 188
Bertrand Freres, Inc. 150

Carr-Lowrey Glass Co. 184
Cavalla, Inc., A. 255
Chiris Co., Inc., Antoine 126
Chrystal Co., Inc., Charles B. 233
Clintbrook Chemical Co., Inc. 251
Colonial Applicator Co. 198
Colton Co., Arthur 246
Columbia-Southern Chemical Corp. 139
Continental Oil Co. ....Facing 139
Crown Cork & Seal Co., Inc. 178

Delta Chemical Works 255
Distillation Products Industries 131
Dodge & Olcott, Inc. 143
Dragoco, Inc. ....Bet. 146-147
Drug & Cosmetic Catalog—1958-59 Edition ....Facing 189
du Pont de Nemours & Co., Inc. 174, 192
Durlin Co. ....Facing 154
Duveen Soap Corp. 123

Eastman Chemical Products, Inc. 219
Emery Industries, Inc. 129
Ertel Engineering Corp. 251

Fairmount Chemical Co., Inc. 255
Federal Paper Board Co., Inc. ....Facing 180
Felton Chemical Co., Inc. ....Facing 130
Filpaco Industries—The Filter Paper Co. 244
Firmenich, Inc. 222

Florasynth Labs., Inc. 138

Gane's Chemical Works 226
General Chemical Div., Allied Chemical Corp. 183
Gifford-Wood Co. 235
Givaudan-Delawanna, Inc. ....Bet. 154-155
Goldschmidt Chemical Corp. 127
Goodrich Chemical Co., The B. F. 136
Gottscho, Inc., Adolph 225
Griffin-Rutgers, Inc. 255

Halby Products Co. 242
Harchem Div., Wallace & Tiernan, Inc. 256
Haring Equipment Corp. 232
Hazel-Atlas Glass—Div. of Continental Can Co. 172
Helfrich Labs. 247
Hoffmann-La Roche, Inc. ....Facing 147, 216
Huisking & Co., Charles L. 251

Kelco Co. 241
Kessler Chemical Co. 231
Knox Glass, Inc. 191

Lee Metal Products Co. 212
Leonhard Wax Co., Theodor 255

Mallinckrodt Chemical Works ....Facing 155
Merck & Co., Inc. 132-133

Neuman, Buslee & Wolfe 232
New York Quinine & Chemical Works ....Facing 131
Norda Essential Oil & Chemical Co. ....Cover 2

Oil Equipment Labs., Inc. 219
Old Empire, Inc. 225
Owens-Illinois Glass Co. ....Facing 197

Penick & Co., S. B. 203
Pennsylvania Glass Products Co., Inc. 190
Pfaltz & Bauer, Inc. 255
Pfizer & Co., Inc., Charles ....Cover 4
Pittsburgh Lectrodryer Corp. 208
Pneumatic Scale Corp., Ltd. 210

Read Standard, A Div. of Capitol Products Corp. 206
Reheis Co., Inc. 130
Rhodia, Inc. 194
Richford Corp. 236
Risdon Manufacturing Co., The ....Facing 181
Ritter & Co., F. 253
Ross & Son Co., Inc., Charles 239
Roure-Dupont, Inc. ....Bet. 138-139

Schimmel & Co. 134
Sheffield Tube Corp., The ....Facing 196
Shell Chemical Corp. ....Facing 146
Shulton, Inc. 148
Sindar Corp. ....Facing 221
Staley Manufacturing Co., A. E. 245
Standard Oil Co. (Indiana) 125
Standard Pharmacal Co. 233
Stepan Chemical Co. 153
Sterwin Chemicals, Inc. 255
Stokes Corp., F. J. 204
Synarome Corp. of America 249
Synfleur Scientific Labs., Inc. 128

Tombarel Products Corp. 243

Ungerer & Co. ....Cover 3
Union Carbide Chemicals Co. 135
Upjohn Co., The 137
U. S. Bottlers Machinery Co. 237

van Ameringen-Haebler, Inc. 140-141
Verley & Co., Albert 215
Verona Chemical Co. ....Facing 220

Wallace & Tiernan, Inc. 256
Welch, Holme & Clark Co. 249
Western Condensing Co. 142
Will & Baumer Candle Co., Inc. 242
Witco Chemical Co. 240
Wolf & Co., Jacques 244